R
SR
4-5
.P16

THE NATIONAL CLEARINGHOUSE FOR MENTAL HEALTH INFORMATION

NATIONAL INSTITUTE OF MENTAL HEALTH

VOL. 13 NO. 3 January 1976

PSYCHOPHARMACOLOGY ABSTRACTS

OWN DRAIN
MAY 21 1976
U N UNIVERSITY

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION

PSYCHOPHARMACOLOGY ABSTRACTS is a publication of the National Clearinghouse for Mental Health Information of the National Institute of Mental Health. It is a specialized information medium designed to assist the Institute in meeting its obligation to foster and support laboratory and clinical research into the nature and causes of mental disorders and methods of treatment and prevention. Specifically, this information service is designed to meet the needs of investigators in the field of psychopharmacology for rapid and comprehensive information about new developments and research results. For information or correspondence with the National Institute of Mental Health concerning *Psychopharmacology Abstracts*, changes of address, or removal of names from the mailing list see the inside back cover page.

The Secretary of Health, Education, and Welfare has determined that the publication of this periodical is necessary in the transaction of the public business required by law of this Department. Use of funds for printing this periodical has been approved by the Director of the Office of Management and Budget through December 31, 1976.

Volume 13, Number 3 January 1976

CONTENTS

Page

ABSTRACTS 191

Preclinical Psychopharmacology

01 Chemical Synthesis, Isolation and Characterization 191
02 Drug Development (Preclinical Screening) 192
03 Mechanism of Action - Physiological, Biochemical and Pharmacological 194
04 Mechanism of Action - Behavioral 229
05 Toxicology and Side Effects 244
06 Methods Development 245

Clinical Psychopharmacology

07 Early Clinical Drug Trials 248
08 Drug Trials in Schizophrenia 248
09 Drug Trials in Affective Disorders 254
10 Drug Trials in Neuroses 262
11 Drug Trials in Miscellaneous Diagnostic Groups 266
12 Psychotomimetic Evaluation Studies 273
13 Mechanism of Action - Physiological, Biochemical and Pharmacological 274
14 Mechanism of Action - Behavioral 278
15 Toxicology and Side Effects 285
16 Methods Development 290

17 *Miscellaneous* 292

AUTHOR INDEX A-13

SUBJECT INDEX S-161

Psychopharmacology Abstracts, is arranged in seventeen categories so that readers may focus more readily on their areas of interest. The Subject and Author Indexes refer the user to the categories under which the abstracts will be found. Thus, in the number 097961 11-14 , the first six digits refer to the abstract number, "11" refers to the issue of *Psychopharmacology Abstracts,* and "14" refers to the category

Carrie Lee Rothgeb, *Editor*
Bette L. Shannon, *Managing Editor*

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

Alcohol, Drug Abuse, and Mental Health Administration
National Clearinghouse for Mental Health Information
5600 Fishers Lane
Rockville, Maryland 20852

Publication No. (ADM) 76-150
Printed 1976

For sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402. Subscription price per year in the United States, Canada, and Mexico: $16.90; other countries, $21.15. Single copy $3.50. Cumulative Index issue $2.25. The Clearinghouse does not sell copies of *Psychopharmacology Abstracts.* Persons wishing to subscribe by the year or to purchase single copies should send their orders, accompanied by check or money order, directly to the Superintendent of Documents.

ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

206460 Soliman, Sobhi A.; Abdine, Hassan; Zakhari, Nashaat A. College of Pharmacy, University of Alexandria, Alexandria, Egypt **Chemistry of nonaqueous titration of chlorpromazine.** Journal of Pharmaceutical Sciences. 64(1):129-132, 1975.

The chemistry of the red color formed during perchloric acid titration of chlorpromazine hydrochloride in acetic acid in the presence of mercuric acetate is discussed. Addition of ascorbic acid prevents the color formation and allows titration using a crystal violet endpoint. Ascorbic acid addition also sharpens the potentiometric endpoint. Ascorbic acid and its oxidation product, dehydroascorbic acid, being neutral to perchloric acid, do not interfere with the titration. 23 references. (Author abstract)

207496 DoAmaral, Jefferson R.; Elliott, Glen R.; Erdelyi, Elizabeth; Wyatt, Richard J.; Renson, Jean; Barchas, Jack D. Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94305 **1-N-methylated tryptamine derivatives: synthesis and properties.** Stanford, CA, Stanford University School of Medicine, 1975. 15 p.

Several 1-N-methyl derivatives of tryptamines were synthesized. The synthetic routes are described and detailed experimental conditions are reported. Melting points, refractive indices, thin layer chromatography, infrared, ultraviolet, spectrophotofluourometric, nuclear magnetic resonance, and mass spectrometric data are given. This appears to be the first report of 1-N-methyl-omega-N,N-dimethyltryptamine methiodide. 21 references. (Author abstract modified)

208592 Bruderlein, Francois T.; Humber, Leslie G.; Voith, Katherine. Dept. of Chemistry, Ayerst Research Laboratories, Montreal, Quebec, Canada **Neuroleptic agents of the benzocycloheptapyridoisoquinoline series. 1.Syntheses and stereochemical and structural requirements for activity of butaclamol and related compounds.** Journal of Medicinal Chemistry. 18(2):185-188, 1975.

The syntheses and the structural and stereochemical requirements fo antagonism of amphetamine induced stereotypy are described for a series of benzyocycloheptapyridoisoquinoline derivatives. One of these compounds, butaclamol hydrochloride, is currently being studied in man. The relationship between structure and antiamphetamine activity in this class of compounds is discussed. 30 references. (Author abstract)

208595 Kalish, Robert; Steppe, Thomas V.; Walser, Armin. Chemical Research Dept., Hoffmann-LaRoche Inc., Nutley, NJ 07110 **Quinazolines and 1,4-benzodiazepines. 67. 5-ferrocenyl-1,4-benzodiazepin-2-ones.** Journal of Medicinal Chemistry. 18(2):222-224, 1975.

Synthesis and properties of 1,4-benzodiazepin-2-ones containing a ferrocenyl group in the 5 position are reported. These compounds are the first stable diazepines containing an organometallic substituent. Preparation and evaluation of the central nervous synthesis activity of these 5-ferrocenyl-benzodiazepinones were examined. The reported similarity of many of the physical and chemical properites of the phenyl and ferrocenyl groups is noted. 6 references.

210352 Morin, R. D.; Benington F.; Mitchell, S. R.; Beaton, J. M.; Bradley, R. J.; Smythies, J. R. University of Alabama Medical Center, University Station, Birmingham, AL 35294 **The behavioral effects of 2,5-dimethoxy-4-alkyl amphetamines.** Experientia (Basel). 31(1):93-95, 1975.

To elucidate the critical function of 4-substitution in 2,5-dimethoxy-4-methylamphetamine (DOM), a series of analogues was synthesized and tested in the rat using a modified Discriminated Sidman Avoidance Schedule. The results indicate that the most potent 4-substituents are n-propyl and n-butyl which are closely followed by methyl and ethyl. The peripheral pharmacology of these substances is obviously quite different from their central nervous system properties, suggesting a unique 5-hydroxytryptophan receptor in the brain. 14 references.

210746 Horn, Alan S.; Post, Michael L.; Kennard, Olga; Di Sanseverino, L. Riva. M.R.C. Neurochemical Pharmacology Unit, Department of Pharmacology, Medical School, Hills Road, Cambridge, England **A crystallographic and theoretical study of the conformation of DOET and its significance for the hallucinogenic amphetamines.** Journal of Pharmacy and Pharmacology (London). 27(1):13-17, 1975.

The crystal and molecular structure of 2,5-dimethoxy-4-ethyl-alpha-methyl -phenylethylamine (DOET) was determined by X-ray crystallography, and the conformation of the side chain was examined theoretically by the use of a potential energy calculation. There was no indication in the solid state of any intramolecular or intermolecular hydrogen bonding. The isopropylamine side chain was staggered to the plane of the benzene ring. The alpha-methyl group was fully extended (antiplanar) whereas the amino group was orientated back towards the ring (synclinal). The potential energy calculations showed the existence of six minima, one of which corresponded to the crystal position. The calculations also showed that the energy differences between the various minima of the side chain were very small. The relationship of these data to the conformations of the hallucinogens, mescaline and 2,4,5-trimethoxyamphetamine is discussed. 19 references. (Author abstract)

210773 Dionyssiou, A.; Miras, C. J. Department of Biological Chemistry, University of Athens School of Medicine, Goudi Athens (609), Greece **Fluorescence of cannabinoids.** Journal of Pharmacy and pharmacology (London). 27(2):135-137, 1975.

The use cannabinoid fluorescence induced by thermal treatment for the identification of cannibis constituents is described. The first morning urine of six regular cannabis users who were subjected to smoking 200mg of cannabis in the evening was collected separately. Seventy five ml of urine from each individual were acidefied to pH3-4 and extracted with an equal volume of light petroleum. The organic layer was collected, the solvent removed under reduced pressure, and the residue thermally treated for delta9-tetrahydrocannabinol (THC). The light petroleum extracts gave essentially the same fluorescence spectra as the thermally treated original THC. The same procedure was followed for urine specimens taken from fifty individuals used as controls. Most of these controls were regular tobacco smokers. The fluorescence spectra of the urine from tobacco smokers did not show any interfering peaks. 3 references.

210895 Linton, Patrick H.; Kuechenmeister, Craig A.; White, Hilton B.; Travis, Robert P. Department of Psychiatry, University of Alabama, Birmingham, AL 35294 **Marijuana: heart rate and EEG response.** Research Communications in Chemical Pathology and Pharmacology. 10(2):201-214, 1975.

Changes in heartrate (HR) and electroencephalogram (EEG) under different doeses of marihuana and delta9-tetrahydrocannabinol (THC) were examined. Subjects (Ss) were kept constantly alert by being involved in problem-solving tasks. HR and EEG recordings were analyzed by time locked evoked averaging techniques. The presentation of each problem task was under computer control and depended on the Ss' return to baseline level of physiological functioning. EEG and HR patterns were shown to be significantly related to dose levels and to the different tasks being performed. The results suggest that marihuana interferes very little with cognitive functions except for impairing short-term memory at all dose levels of marihuana. The procedure described for the measurement of Ss' HR and EEG changes while they are alert as they respond to various perceptual stimuli, and for the analyses of these changes, offers a particularly powerful technique for looking at subtle drug treatment effects not only of marihuana but also of other drugs. 12 references. (Author abstract modified)

211069 Winn, M.; Horrom, B. W.; Rasmussen, R. R.; Chappell, E. B.; Plotnikoff, N. P. Division of Pharmacology and Medicinal Chemistry, Abbott Laboratories, North Chicago, IL 60064 **N-cyclopropyltryptamines, potent monoamine oxidase inhibitors.** Journal of Medicinal Chemistry. 18(4):437-438, 1975.

The pharmacology of N-cyclopropyltryptamines which are potent monoamine oxidase (MAO) inhibitors is described. Only structure one showed MAO inhibitory properties. The most potent was the unsubstituted compound 3a, which was even more potent than pargyline. However, 3a was equally potent with tryamine as a substrate as it was for tryptamine. These compounds were tested for potentiation of the behavioral effects of 5-hydroxytryptophan (5-HTP) in mice. Compound 3a showed marked potentiation of 5-HTP at 10, 25, and 100mg/kg orally. Compound 3c showed marked potentiation of 5-HTP at 10, 25, and 100mg/kg and moderate potentiation at 5mg/kg. However 3b, the compound which is the closest analog of serotonin, did not potentiate 5-HTP even at 100 mg/kg. Mouse symptomatology for these compounds showed tremors, decreased motor activity, ataxia, and dilation of blood vessels. Compound 3c did not show tremors or decreased motor activity until 100 mg/kg (oral dose) with no dilation of blood vessels. This vasodilation was noted as a reddening of the ears of the mice. 11 references. (Author abstract modified)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

206438 Andreeva, N. I.; Altikhova, L. B.; Grineva, A. N.; Mashkovskiy, M. D.; Shvedov, V. I. Vsesoyuznogo nauchno-issledovatel'skogo khimiko-farmatsevticheskogo instituta im. S. Ordzhonikidze, U.S.S.R. /**An investigation of psychotropic activity in a series of piperazine (1,2-a) indole derivatives.**/ Issledovaniye psikhotropnoy aktivnosti v ryadu proizvodnykh piperazino (1,2-a) indola. Farmakologiya i toksikologiya (Moskva). 37(5):524-528, 1974.

The psychotropic activity of five new piperazine derivatives was investigated in male albino mice. The Chane method was used to measure the influence of piperazine preparations on the toxicity of phenamine. The 1,10-trimethylene derivatives of the piperazine series displayed a number of characteristics typical of antidepressants; they intensified the central effect of phenamine, weakened reserpine activity, and negated the hypothermic effect. Psychotropic piperazine derivative activity was, however, found to be weaker than normal for antidepressants. 5 references. (Journal abstract modified)

206461 Parmar, Surendra S.; Gupta, A. K.; Gupta, T. K.; Stenberg, Virgil I. University of North Dakota, Dept. of Physiology and Pharmacology, School of Medicine, Grand Forks, ND 58201 **Synthesis of substituted benzylidinohydrazines and their monoamine oxidase inhibitory and anticonvulsant properties.** Journal of Pharmaceutical Sciences. 64(1):154-157, 1975.

Some N1-(4-acetamidobenzoyl)-N2-(substituted phenyl carboxylate) benzylidinohydrazines were synthesized, characterized, and evaluated for their ability to inhibit monoamine oxidase in vitro. All substituted benzylidinohydrazines inhibited monoamine oxidase activity of rat brain homogenates. These compounds possessed anticonvulsant activity, which was reflected by the protection afforded against pentylenetetrazol induced convulsions; they also potentiated pentobarbital induced hypnosis in mice. Monoamine oxidase inhibitory effectiveness of these substituted benzylidinohydrazines was unrelated to their anticonvulsant activity and their ability to potentiate pentobarbital induced hypnosis. 9 references. (Author abstract)

206780 Asami, Y.; Otsuka, M.; Hirohashi, T.; Inaba, S.; Yamamoto, H. Sumitomo Chemical Co., Ltd., Osaka, Japan **The synthesis and pharmacology of a novel benzodiazepine derivative, 1-methyl-5-(o-flurophenyl)-7-chloro-1,3-dihydro-2H-1,4-benzo odiazepin-2-one (ID-540).** Arzneimittel-Forschung (Aulendorf). 24(10):1563-1568, 1974.

A new benzodiazepine derivative, ID-540, was evaluated in pharmacological tests on the central nervous system and acute toxicity studies. Findings indicate that ID-540 has pharmacological properties similar to well known benzodiazepine derivatives such as diazepam. Moreover, ID-540 is characterized by marked anticonvulsant and taming effects. Indications that ID-540 has potent antianxiety activity have been confirmed in recent human trials. ID-540 has a weak toxicity in mice. 26 references. (Author abstract modified)

206804 Niemegeers, C. J. E.; Janssen, P. A. J. Dept. of Pharmacology, Research Laboratoria, Janssen Pharmaceutica, B-2340 Beerse, Belgium **Bromoperidol, a new potent neuroleptic of the butyrophenone series; comparative pharmacology of bromoperidol and haloperidol.** Arzneimittel-Forschung (Aulendorf). 24(1):45-52, 1974.

The comparative pharmacology of bromoperidol, a new potent neuroleptic of the butyrophenone series, and haloperidol is described on the basis of studies in rats, mice and dogs. In animals the pharmacological profile of bromoperidol resembles that of haloperidol. Bromoperidol is very potent by the oral route and has a duration of at least 24 hours at four times the minimum effective dose 50 value of the antiapomorphine test in dogs. Onset of action of bromoperidol is very fast after subcutaneous injection and gradual and smooth after oral administration, reaching a peak between four and eight hours. Bromoperidol is relatively atoxic. Qualitatively bromoperidol is closely related to haloperidol. Reversible neuroleptic side-effects are expected to occur when overdosed; somnolence or drowsiness is expected to be extremely rare; and orthostatic hypotension should be no problem. 12 references. (Author abstract modified)

VOLUME AND ISSUE NUMBER INCORRECT
SHOULD READ VOL.13, ISSUE 3

206808 Allen, L. E.; Ferguson, H. C.; Cox, R. H., Jr. Mead Johnson Research Center, Dept. of Pharmacology, Evansville, IN 47721 **Pharmacologic effects of MH 9022-1, a potential tranquilizing agent.** Arzneimittel-Forschung (Aulendorf). 24(6):917-922, 1974.

A pharmacolological study of MJ-9022-1 (buspirone hydrochloride) is reported which indicates that the agent has psychotropic and antiemetic properties comparable to those of major tranquilizers. In rats, it selectively suppresses the conditioned avoidance response (CAR) in the barrier jump test and free operant behavior in a continuous avoidance schedule. Tolerance did not develop to depression of the CAR with repeated oral administration of MJ-9022-1, while tolerance was observed with chlorpromazine (CPZ). The tranquilizing action of MJ-9022-1 has been confirmed in mice and monkeys, although the potency is somewhat less than that observed in rats. The activity of MJ-9022-1 is evident by both oral and parenteral administration. Duration of action is less than that of CPZ. MJ-9022-1 appears to 1) possess minimal sedative effects; 2) induce only mild hypothermia; and 3) essentially lack antinociceptive activity and alpha-adrenergic receptor blocking properties at effective tranquilizing doses. 15 references. (Author abstract modified)

206994 Gutsche, K.; Schroder, E.; Rufer, C.; Loge, O. 2084 Rellingen, Ehmscherkamp Nr.5, Germany **/New hypoglycemic benzenesulfonamido-pyrimidines: N-substituted 4-(N-(2-pyrimidinyl)sulfonyl)-phenylacetamides.** Neue blutzuckersenkende Benzolsulfonamido-pyrimidine: N-Substituierte 4-(N-(2-Pyrimidinyl)-sulfamoyl)-phenylessigsaureamide. Arzneimittel-Forschung (Aulendorf). 24(7):1028-1039, 1974.

The synthesis of new benzenesulfonamido-pyrimidines, N-substituted 4-(N-(2-pyrimidinyl)sulfamoyl)phenylacetamides with a strong hypoglycemic activity is reported. Phenylacetanilides, phenylacetbenzylamides and phenylacet-(1-phenylethylamides) proved to be especially effective, causing a blood sugar reduction of more than 25% in rabbits. These compounds have an activity in these animal species more than 100 times that of formerly described pyrimidines of the glymidine type. By means of a selected series of compounds, the structure - activity relationship and also a comparison with blood sugar reducing compounds of the acylaminoakylbenzenesulfonylureas and aminopyrimidines are discussed. 11 references. (Author abstract)

207164 Singh, K. P.; Bhandari, D. S. Dept. of Pharmacology, R.N.T. Medical College, Udaipur/Rajasthan, India **Experimental study on neuropharmacological actions of some indole derivatives.** Arzneimittel-Forschung (Aulendorf). 23(7):973-977, 1973.

The neuropharmacological effects of three indole derivatives, 3-indole-methanol-alpha-(dimethyl-aminomethyl-N-oxide)-1-methyl (U-7582), 3-indole-methanol-alpha-(dimethyl-aminomethyl)-1-methyl (U-5092) and 2-(indol-3-ylmethyl)-amino-ethanol (U-13625), along with 5-hydroxytryptamine (serotonin, 5-HT) as a standard were investigated in rats by utilizing a variety of test procedures in order to give more credence to the results. Results reveal that the drugs possess barbiturate hypnosis potentiating effect, analgesic effect, anticonvulsant effect, antitremor effect, hypothermic effect and tranquilizing effect. The significance of these observations is discussed in the light of present test results. 18 references. (Author abstract modified)

208594 Uliss, D. B.; Dalzell, H. C.; Handrick, G. R.; Howes, J. F.; Razdan, R. K. Sheehan Institute and Sharps Associates, Cambridge, MA 02138 **Hashish. Importance of the phenolic hydroxyl group in tetrahydrocannabinols.** Journal of Medicinal Chemistry. 18(2):213-215, 1975.

Optically active delta9-tetrahydrocannabinol (THC) and delta8-THC, cannabidiol and racemic delta9-cis-THC, and their corresponding analogs in which the positions of the phenolic hydroxyl group and the n-C5 side chain have been interchanged are compared in selected pharmacological tests in mice. The results indicate that the phenolic hydroxyl group in the 1 position in THC's is very important for eliciting activity and that cannabidiol and delta9-cis-THC possess weak central nervous system depressant properties. 17 references. (Author abstract)

210676 Johnson, D. N.; Funderburk, W. H.; Ward, J. W. A. H. Robins Research Laboratories, Richmond, VA 23220 **Preclinical evaluation of AHR-2244: a new psychotherapeutic agent.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 211(2):326-340, 1974.

AHR-2244 a new nonphenothiazine, nonbutyrophenone agent with potential major tranquilizing and sedative properties is described. Conditioned avoidance responding was blocked in mice, rats, and cats in doses which did not markedly alter escape behavior. The drug suppressed amphetamine induced lethality in mice under aggregated conditions in doses comparable to those of other major tranquilizers. Evidence of dopamine blockade in the corpus striatum was seen in mice and rats. Oral or parenteral administration of AHR-2244 potentiated hexobarbital sleeping times in mice. Electroencephalographic parameters in unanesthetized, paralyzed cats suggested the drug was similar in action to haloperidol but with more sedative properties. 11 references. (Author abstract)

210811 Laduron, Pierre. Department of Neurobiochemistry, Janssen Pharmaceutica, B-2340 Beerse, Belgium **Scope and limitation in dopamine beta-hydroxylase measurement.** Biochemical Pharmacology (Oxford). 24(5):557-562, 1974.

The scope and limitation in dopamine beta-hydroxyalase measurement are discussed. The methodology in the measurement of DBH is limited by the lack of substrate specificity for p N-methyltransferase (PNMT), the choice of a blank in measuring DBH by a coupled reaction and the presence of endogenous inhibitors of DBH. Factors such as age, the influence of drugs, and enzyme kinetic parameters are important in sources of error. 35 references.

210870 Fuller, R. W.; Perry, K. W.; Baker, J. C.; Molloy, B. B. Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN 46206 **6-Cholor-2-aminotetralin, a rigid conformational analog of 4-chloroamphetamine: pharmacologic properties of it and related compounds in rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 212(1):141-153, 1974.

The pharmacologic properties of 6-cholor-2-aminotetralin, a rigid conformational analog of 4-chloramphetamine were examined in the rat. The drug lowered both 5-hydroxytryptamine and 5-hydroxyindoleacetic acid levles in rats. Other chlorinated 2-aminotetralins with chloro substituents in the 5-, 6-, 7-, or 8-positions of the benzene ring had differential effects on brain levels of 5-hydroxytryptamine and 5-hydroxyindoleacetic acid. They inhibited monoamine oxidase to varying degrees in vitro and apparently in vivo. Brain levels and half lives of the chlorinated 2-aminotetralins depended on the position of lives of the chlorinated 2-aminotetralins depended on the position of the chloro substituent and, in certain cases,

were increased by an inhibitor of aromatic hydroxylation. Thus both metabolism and 5-hydroxyindole effects of the chlorinated 2-aminotetralins resemble those of chlorinated amphetamines. The results with chlorinated 2-aminotetralins as rigid conformational analogs of chloroamphetamines strenghten the concept that these agents affect brain 5-hydroxyindoles through multiple actions on 5-hydroxytryptamine uptake, relase, and metabolism. 14 references. (Author abstract)

210878 Sofia, R. D.; Knobloch, L. C. Wallace Laboratories, Department of Pharmacology, Cranbury, NJ 08512 **The effect of delta9-tetrahydrocannabinol pretreatment on ketamine, thiopental or CT-1341 -- induced loss of righting reflex in mice.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 207(2):270-281, 1974.

The effects of delta9-tetrahydrocannabinol (THC) pretreatment on ketamine, thiopental or CT-1341 were examined. Pretreatment with a fixed dose of THC produced a significant increase in the duration of action and number of mice exhibiting loss of the righting reflex when given 30 min prior to administration of ketamine HCl, Na thiopental or the steroidal anesthetic CT-1341. Pretreatment with a similar dose of THC did not alter the LD50 of any of these anesthetic agents. Duration of the THC effect on each drug persisted for up to 120 min with peak effect differing depending on absorption times. When mice were pretreated with various doses of THC prior to a fixed dose of a particular anesthetic they displayed dose dependent elevations in sleeping time. 26 references. (Author abstract modified)

210882 Heikkila, Richard E.; Cohen, Gerald; Manian, Albert A. Mt. Sinai School of Medicine, Fifth Ave. at 100th St., New York, NY, 10029 **Reactivity of various phenothiazine derivatives with oxygen and oxygen radicals.** Biochemical Pharmacology (Oxford). 24(3):363-368, 1975.

7,8-Dihydroxychlorpromazine, 7,8-dihydroxyprochlorperazine and 7,8-dihydroxyperphenazine all reacted with O2 to make hydrogen peroxide (H2O2). The rate of reaction between the ortho-dihydroxyphenothiazines and O2 was increased by superoxide dismutase, an enzyme which catalyzes the dismutation of the superoxide radical (O2-) to H2O2 and O2. This indicated the formation of oxygen ion during the autoxidation of the ortho-dihydroxyphenothiazines. Several phenothiazines lacking the ortho-dihydroxy groups did not consume O2 at a detectable rate (did not generate H2O2). All ortho-dihydroxyphenothiazines tested also reacted with O2 in the presence of methional to form ethylene. Ethylene formation was inhibited by catalase and hydroxyl radical (OH) trapping agents, such as sodium benzoate; this indicated OH formation from the ortho-dihydroxyphenothiazines. Several nonhydroxylated phenothiazines and monohydroxylated phenothiazines inhibited ethylene generation from 6-aminodopamine, which also generates OH. This inhibition was probably mediated by a reaction between the phenothiazine and OH. All of the above reactions may be responsible for some of the beneficial and/or adverse effects of administered phenothiazines. 26 references. (Author abstract)

211071 Tuck, J. Richard; Kahan, Elisabeth; Siwers, B. Department of Psychiatry, Karolinska Institutet, Sweden **Biological and pharmacokinetic evidence for generic equivalence of three imipramine preparations: comparison with a new imipramine analogue.** Acta Pharmacologica et Toxicologica (Kobenhavn). 32(3-4):304-313, 1973.

The biological availability of three imipramine preparations and an imipramine analogue, Leo 640, was studied using a recently developed biological procedure. The isolated rat iris, was used to elucidate the inhibitory power of these drugs on noradrenaline uptake into adrenergic nerve terminals. Irides incubated in patients' plasma before and during drug treatment were compared in two series of cross-over studies on hospitalized patients. It was found that the drugs compared seemed to be identical with regard to their effect on noradrenaline neurons. It has been hypothesized that the antidepressive effect of this type of tricyclic drugs is brought about by their inhibition of reuptake of monoamines released into central synapses. This method provides a new way for comparing these drugs and their active metabolites at the presumed site of action. 27 references. (Author abstract)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

205604 Benesova, O.; Benes, V. Medical Faculty of Hygiene, Charles University, Praha 10, Srobarova 50, Czechoslovakia **The effect of maprotiline on brain serotonin metabolism in rats.** Activitas Nervosa Superior (Praha). 16(3):190-191, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, describes the effects in rats of maprotiline on the metabolism of brain serotonin, which is considered to play an important role in the mechanism of antidepressant action. Maprotiline reveales quite a different pharmacological profile than classical tricyclic antidepressants. Its antireserpinic and central anticholinergic activities are very low. It has significant serotoninomimetic action, which is of different quality, probably resulting in an increased serotonin synthesis and not in inhibition of serotonin uptake. 12 references.

205625 Sklenovsky, A.; Navratil, J.; Hrbek, Jan; Krejci, Z. Department of Pathophysiology, Medical Faculty UP, Olomouc, Dr. S. Allende 3, C.S.S.R. **Effect of delta-9-tetrahydrocannabinol on free amino acids in brain.** Activitas Nervosa Superior Praha). 16(3):216-217, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, reports an experiment in which the later phase of the effects of delta9-tetrahydrocannabinol (THC) administered to rats was reported in tissue slices. The changes in release of glutamic acid (GA), glutamine (GL) and gamma-aminobutyric acid (GABA) from brain cortex were studied. The changes of the membrance permeability and of amino acids could be partly explained by charging that the THC exerted an uncoupling effect upon respiration and decreased adenosine diphospate to oxygen ratio. THC released matrix enzymes from liver mitochondria and destabilized some phospholipid in artificial membranes. 5 references.

205629 Sikora, J.; Krulik, R. Psychiatric Research Laboratory, Praha 2, Ke Karlovu 11, Czechoslovakia **Psychotropic drugs and differently stimulated ATPase in CNS.** Activitas Nervosa Superior Praha). 16(3):222-223, 1974.

At the 16th Annual Psychopharmacological Meeting, a study of the effects of drugs from the phenothiazine series was reported on differently stimulated ATPase. It was proved that chlorpromazine and amitriptyline inhibit Mg++, Na+ K+ and C++ ATPase competitively. A hypothesis was advanced about the possible reaction of these psychotropic drugs with polyphosphates. The effects of chlorpromazine on the activity of Mg++ ATPase of differently solubilized (water triton) mitochondrial and synaptosomal fractions was examined. Solubilization did not change inhibition in the mitochondrial fraction, while in synaptosomes inhibition was greatest in the non-solubilized preparations (saccharose). In vivo experiments on

rats have shown that a single application of chlorpromazine in a dose of 16mg/kg induced a significant drop in Mg++ as well as Na+K+ ATPase. Amitriptyline produced a decline soley in Mg++ ATPase. An application of chlorpromazine in a dose of 8mg/kg for 10 days elicited no significant changes, while amitriptyline in the same dose reduced the activity of Mg++ ATPase and of Na+K+ ATPase. 2 references.

205630 Farska, I.; Krulik, R. Psychiatric Research Laboratory, Praha 2, Ke Karlovu 11, Czechoslovakia **Psychotropic drugs and some enzymes of energy metabolism.** Activitas Nervosa Superior Praha). 16(3):223-224, 1974.

At the 16th Annual Psychopharmacological Meeting, the effects of chlorpromazine, amitriptyline, imipramine, chlordiazepoxide and lithium on the activity of adenylate kinases in vitro and of creatine kinases in vitro and in vivo in rats were reported. The fractions obtained were tested electronoptically as well as by determining acetylcholinesterase and succinatedehydrogenase. Chlordiazepoxide had no effect on activity. The curve of inhibition for chlorpromazine in dependence on various concentrations of the substrate indicates a competitive inhibitory effect. Chlorpromazine in a dose of 16mg/kg and amitriptyline in a dose of 8mg/kg did not affect significantly the activity of creatine kinase, either after a single or after applications of 8 and 10 days. 4 references.

205631 Rump, S.; Rabsztyn, T.; Kopec, J. Department of Toxicology, Military Institute of Hygiene, Kozielska 4, 00-967 Warszawa, Poland **Effects of cholinesterase inhibition on the visual evoked potentials in the rabbit and their modification with various drugs.** Activitas Nervosa Superior Praha). 16(3):224-225, 1974.

At the 16th Annual Psychopharmacological Meeting, a study of the central effects of anticholinesterases and their antagonists in 25 rabbits with chronically implanted skull electrodes over the visual cortex was reported. The decrease of amplitude of visual evoked potential (VEP) was observed earlier than the desynchronization of cortical activity. The effects of cholinolytics on the abnormalities of VEP induced by cholinesterase inhibition were clearest. Diethazine had an effect which looks like near complete normalization of VEP, though it had no influence on cortical activity in these situations and in tested doses. The actions of diazepam on the early stage of VEP did not reflect on the activity of the cortex. It is suggested that the mechanisms which induce changes of the background electrocorticogram are different from those which affect evoked potentials.

205632 Herink, J.; Bajgar, J.; Nemecek, S.; Golda, V.; Fusek, J.; Patocka, J.; Hrdina, V. Faculty of Pharmacy, 500 27 Hradec Kralove, Czechoslovakia **Some factors determining the response of septal rats to anticholinergic drugs.** Activitas Nervosa Superior Praha). 16(3):225-226, 1974.

At the 16th Annual Psychopharmacological Meeting, an investigation of the sensitivity of normal and septal rats to anticholinergic drugs was reported. It was suggested that this different sensitivity should be related to an alteration of the blood - brain barrier as a consequence of surgical procedure or to an intervention in the specific neuronal mechanisms. Small electrolytic lesions of the dorsal septum were made and acetylcholinesterase (AChE) activity of the hippocampus, septum, thalamus, hypothalamus, amygdala, cingulate and frontal cortex was compared with normal and sham operated animals. In septum, hypothalamus and amygdala no changes were found. In hippocampus, thalamus, frontal and cingulate cortex there were significantly lower values of AChE in comparison with both control groups. It is concluded that the circuits between septum, hippocampus, thalamus and supracallosal cortex are important for the central action of anticholinergic drugs. 3 references.

205851 Patel, Girish J.; Schatz, Robert P.; Constantinides, Spiro M.; Lal, Harbans. Department of Pharmacology and Toxicology, University of Rhode Island, College of Pharmacy, Kingston, RI 02881 **Effect of desipramine and pargyline on brain gamma-aminobutyric acid.** Biochemical Pharmacology (Oxford). 24(1):57-60, 1975.

The effect of desipramine and pargyline on brain gamma-aminobutyric acid (GABA) was studied in mice. Intraperitoneal administration of desipramine or pargyline reliably elevated the brain concentration of GABA in a dose dependent manner. Both drugs caused hypothermia and a prolongation of sodium barbital induced narcosis. None of those effects of desipramine were seen when the treated animals were placed in high ambient temperature to prevent drug induced hypothermia; however, this was not true of pargyline. 27 references. (Author abstract modified)

205852 Slotkin, Theodore A. Department of Physiology and Pharmacology, Duke University Medical Center, Durham, NC 27710 **Maturation of the adrenal medulla -- III: practical and theoretical considerations of age-dependent alterations in kinetics of incorporation of catecholamines and non-catecholamines.** Biochemical Pharmacology (Oxford). 24(1):89-97, 1975.

Rats were sacrificed at 10 day intervals from birth to 50 days of age and the kinetics of uptake of epinephrine (E) and metaraminol (MA) into isolated adrenal medullary storage vesicles were measured. The preference of the vesicles for uptake of E vs MA was approximately six to one at birth, one to one at 10 days, 3.5to one at 20 days, and five to one thereafter, while the preference for E vs tyramine was two to one. These data suggest that the two vesicular uptake mechanisms develop independently of each other. The age dependent alterations are present both at the level of the vesicle membrane and intravesicular storage. 30 references. (Author abstract modified)

205853 Riceberg, Louis J.; Simon, Marcia; Van Vunakis, Helen; Abeles, Robert H. Graduate Department of Biochemistry, Brandeis University, Waltham, MA 02154 **Effects of aminoacetonitrile, an amine oxidase inhibitor, on mescaline metabolism in the rabbit.** Biochemical Pharmacology (Oxford). 24(1):119-125, 1975.

The metabolism of mescaline was examined in the rabbit to determine the effects of aminoacetonitrile. It was found that mescaline rapidly underwent oxidative deamination to 3,4,5-trimethoxyphenylacetic acid in the control and pargyline treated rabbits. In the aminoacetonitrile and proparagylamine treated animals, mescaline oxidation was inhibited and other metabolites were formed. Results indicate that enzymes related to plasma enzymes are primarily responsible for the oxidation of mescaline in the rabbit. 40 references. (Author abstract modified)

206014 Sethi, N.; Sethi, B. B. Central Drug Research Institute, Lucknow, India **A teratogenic study of haloperidol.** Indian Journal of Psychiatry (Madurai). 16(2):165-169, 1974.

Haloperidol was administered to pregnant mice from sixth to fifteenth post-coitus day. It exhibited its effects mainly on the total litter size, weight and resorptions. The effect was max-

imum in animals receiving the highest dose level of 10 mg. kg./day. This indicates an embryotoxic effect of the drug and not a teratogenic effect. 7 references. (Author abstract)

206108 Jacobs, Barry L. no address **Functional-anatomical studies of the raphe nuclei.** Final Report, NIMH Grant MH-24771, 1975, 6 p.

The results of eight studies on serotonin percursors, raphe units, and raphe lesions are reported. Studies of serotonin precursors showed that: (1) at least part of the behavioral effects of 5-hydroxytryptophan (5-HT) may be attributable to peripheral actions; (2) L-tryptophan, even in doses which markedly increase brain 5-HT, has little or no behavioral effect; (3) many of the effects of levodopa (l-dopa) may be mediated by 5-HT rather than by dopamine; and (4) pimozide is a more specific dopamine receptor blocker than spiroperidol which also blocks 5-HT receptors. Results of the raphe unit studies show that peripherally administered 5-HT does not cross the blood - brain barrier as function 5-HT, and that its effects on raphe neurons may be mediated by changes in blood pressure. Lesions of the median raphe nucleus resulted in large increases in locomotor activity and depletion of hippocampal 5-HT: neither of these two effects were seen following lesions of the dorsal nucleus. 7 references. (Author abstract modified)

206250 Koss, M. C. no address **/Reactive brainstem loci for eliciting electrodermal responses./** no title. Final Report, NIMH Grant MH-24083, 1975, 2 p.

Reactive brainstem loci for eliciting electrodermal responses were determined in anesthetized cats. These skin potential changes could be evoked by stimulating an apparently continuous pathway extending from the posterior hypothalamus to the cervical cord. Centrally evoked responses were invariably bilateral and stable in nature, with the largest potential changes in the range of 20 mV to 30 mV. Midline loci and the classical dorsal medullary cardiovascular regions were unreactive. After definition of the excitatory pathway, this system was used as a model with which to segregate the central and peripheral actions of chlorpromazine and reserpine. While reserpine had no effect, chlorpromazine invariably reduced only the central electrodermal response. Preliminary evidence indicates that this central action of chlorpromazine is confined to an area extending from the midbrain to the rostral border of the medulla. (Author abstract modified)

206334 Shellenberger, M. K.; Gordon, J. H. Dept. of Pharmacology, Kansas Univ. Medical Center, Kansas City, KS **Regional differences in response to displacement and inhibition of synthesis of catecholamines in the cat brain.** Biological Psychiatry. 9(2):131-145, 1974.

The effects of synthesis inhibition and displacement on catecholamine concentrations in several brain regions were compared in surgically prepared, immobilized cats. These stressful procedures of preparation were found to significantly lower hypothalamic norephinephreine (NE) as do other stresses in rats. Furthermore, it was demonstrated that cortical NE was also lowered while dopamine (DA) in this region increased. The levels of NE and DA were unchanged in other regions as was the 5-hydroxytryptamine in all regions. Following these acute changes, levels of amines were stable in all areas up to 6 hr after recovery from anesthesia. Subsequent studies with alpha-methyl-m-tyrosine (AMMT), and alpha-methyl-p-tyrosine (AMPT) disclosed remarkable regional differences in the dose - response relationship, time course, and susceptibility of NE and DA to displacement by the metabolites of AMMT. Regional differences were also found in susceptibility to depletion by synthesis inhibition with AMPT as well as regional and intraregional differences when the abilities of both agents to produce depletion were compared. A scheme was proposed to account for regional differences in response to AMMT. Furthermore, these findings confirm and extend to cats the probable existence of at least two stores of DA in the caudate nucleus and suggest a similar circumstance for hypothalamic NE. It is suggested that these two stores may exist in different neuronal populations as well as in the currently postulated intraneuronal "pools."35 references. (Author abstract modified)

206335 Segal, David S.; Kuczenski, Ronald; Mandell, Arnold J. Dept. of Psychiatry, School of Medicine, Univ. of California, San Diego, La Jolla, CA **Theoretical implications of drug-induced adaptive regulation for a biogenic amine hypothesis of affective disorder.** Biological Psychiatry. 9(2):147-160, 1974.

Administration of the tricyclic antidepressant desmethylimpramine (DMI) produced a significant decrease in the activity of regional brain tyrosine hydroxylase in noradrenergic pathways and a marginal decrease in the dopaminergic system of the rat brain. No change in the enzyme activity was observed 24 hr after a single administration of the same drug. In contrast, chronic reserpine treatment induced a delayed elevation of tyrosine hydroxylase activity of varying signfificance in the discrete brain regions examined. The functional significance of these apparent drug induced compensatory responses is discussed in the context of a neurochemical theory of affective disorder that focuses on the role of adaptive regulatory mechanisms. 48 references. (Author abstract)

206336 Extein, Irl; Roth, Robert H.; Bowers, Malcolm B., Jr. Dept. of Psychiatry, Yale Univ. School of Medicine, New Haven, CT **Accumulation of 3H-homovanillic acid in rabbit brain and cerebrospinal fluid following intravenous 3H-L-dopa.** Biological Psychiatry. 9(2):161-170, 1974.

The metabolism of a tracer amount of intravenously injected 3H-L-dopa was studied in rabbits treated with a peripheral decarboxylase inhibitor and probenecid. Radioactive metabolites in the brain and cisternal CSF were separated by thin layer chromatography. Brain dopamine radioactivity was maximal by 30 min and then declined rapidly as 3H-homovanillic acid (HVA), a major dopamine metabolite, accumulated significantly in the brain and CSF over a 4 h period. Accumlation of 3H-HVA roughly paralled that of endogenous HVA in the CSF. Chlorpromazine pretreatment significantly increased the labeled and endogenous HVA in the brain and CSF at 4 h. Thus, the accumlation of 3H-HVA in the CSF increased in response to the increase in central neuronal dopamine metabolism which chlorpromazine is known to cause. Possible application of this method to the study of brain doapmine metabolism in humans is discussed. 39 references. (Author abstract)

206353 Hirschhorn, I. D.; Rosecrans, J. A. Dept. of Pharmacology, Medical College of Virginia, Richmond, VA 23928 **Studies on the time course and the effect of cholinergic and adrenergic receptor blockers on the stimulus effect of nicotine.** Psychopharmacologia (Berlin). 40(2):109-120, 1974.

The stimulus property of nicotine in the rat was investigated to determine: 1) the time course of the nicotine stimulus and its relationship to brain levels of the drug, and 2) whether the nicotine stimulus is dependent upon the integrity of specific neurotransmitter systems. A lever choice discrimination was used, and a high degree of discriminated responding was observed when nicotine was used as a discriminative stimulus.

The degree of discrimination decreased as the length of the time between the injection of nicotine and the test of discrimination was increased. This decline in discrimination was similar to the decline in brain levels of nicotine, suggesting that nicotine discrimination is directly related to the concentration of nicotine in the brain. Atropine, mecamylamine, dibenamine, propranolol and alpha-methyl-para-tyrosine were all tested for effects upon nicotine discrimination, and only mecamylamine antagonized the nicotine stimulus. Results indicate that the stimulus effect of nicotine is mediated specifically through nicotinic cholinergic receptors and not muscarinic cholinergic or adrenergic receptors. 20 references. (Author abstract modified)

206354 Clemens, James A.; Smalstig, E. Barry; Sawyer, Barry D. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Antipsychotic drugs stimulate prolactin release.** Psychopharmacologia (Berlin). 40(2):123-127, 1974.

Antipsychotic drugs were found to markedly stimulate prolactin secretion in male and female rats. The amount of prolactin released was greater in females than in males. Most nonantipsychotic phenothiazines failed to alter prolactin. These results imply that the dopamine receptor that inhibits the prolactin release may be similar to the dopamine receptor involved in the action of antipsychotic drugs. 18 references. (Author abstract)

206359 Pakkenberg, H.; Fog, R. Kommunehospitalet, O. Farimagsgade 5, DK-1399, Copenhagen, Denmark **Short-term effect of perphenazine enanthate on the rat brain.** Psychopharmacologia (Berlin). 40(2):165-169, 1974.

The effect of 1 or 2 month administration of perphenazine enanthate on the rat brain was investigated. Approximately 20% loss of nerve cells had been found in the basal ganglia (but no loss in the cortex) after administration of the same dosage for 12 months. There were 10 animals in both the control and treated groups and five animals from each of the groups were given 3H-uridine intravenously 1 hour prior to being sacrificed. Autoradiographic studies of the uridine uptake in the nerve cells of the cortex and basal ganglia and in the cells of the liver were then performed. No loss of cells was found following cell counts in the cortex and basal ganglia after relatively short-term treatment. The weight of the brain was similar in both the control and treated groups. 2 references. (Author abstract modified)

206365 Sandler, Merton. Queen Charlotte's Maternity Hospital, London W6 0XG, England **/Biochemical background of monoamine oxidase inhibitors./** The new biochemical background. Proceedings of the Royal Society of Medicine (London). 66(9):946-947, 1973.

At the December 12, 1972 meeting of the Royal Society of medicine, the differential effectiveness of monoamine oxidase (MAO) inhibitors was attributed to the fact that MAO has been shown to exist as a mixture of multiple forms, the number of which varies from tissue to tissue. The different forms may be separated electrophoretically, and some evidence suggests that they appear in vivo as well as in vitro. It was hypothesized that specific inhibitors could be developed in the future to treat specific illnesses. Tyramine sensitive migraine was discussed as an example of an enzyme deficiency which may be aggravated by MAO inhibitors. 17 references.

206404 Reprintseva, V. M. Laboratory of General Physiology, Minsk, U.S.S.R. **/Influence of iproniazid on the content of noradrenaline in various parts of the rat brain before and after stimulation of the receptors./** Vliyaniye iprazida na soderzhaniye noradrenalina v raznykh chastyakh mozga krys do i posle razdrazheniya retseptorov. In: Bulygin, I., Neyrogumoral'nyye mekhanizmy reflektornykh reaktsiy. Minsk, Nauka i tekhnika, 1973. 239 p. (p. 77-80).

The influence of iproniazid and mechanical interoceptive and exteroceptive stimulation on the noradrenaline content of various rat brain sections was studied. After administration of iprazid, interoceptive stimulation resulted in increased noradrenaline content in the cortex of the large hemispheres and a decrease in noradrenaline in the cerebellum and middle brain. In control rats, before iproniazid administration, interoceptive stimulation resulted in another reaction -- a decrease in noradrenaline. Exteroceptive stimulation after administration of iproniazid led to a decrease in noradrenaline level except in the cortex of the large hemispheres, whereas in control rats, noradrenaline level was reduced only in the hypothalamus. 13 references.

206415 Kirilyuk, A. P. Laboratory of General Physiology, Minsk, U.S.S.R. **/Influence of reserpine on hemodynamics in dogs./** Vliyaniye rezerpina na gemodinamiku u sobak. In: Bulygin, I., Neyrogumoral'nyye mekhanizmy reflektornykh reaktsiy. Minsk, Nauka i tekhnika, 1973. 239 p. (p. 150-153).

The influence of reserpine on the hemodynamics of dogs was studied. The lowering of arterial pressure operates through different hemodynamic mechanisms in different periods. In the beginning (first 5 days) its effect stems from reducing general peripheral resistance of vessels despite an increase in volume of blood (vascular form of hypotension). Further reduction of vascular pressure comes from a reduction in heart pumping (mixed form of hypotension). 12 references.

206441 Kozhechkin, S. N. no address **/Microiontophoretic studies on the effect of norepinephrine on the activity of the visual cortex neurons in rabbits./** Mikroionoforeticheskoye izuncheniye vliyaniya noradrenalina na aktivnost' neyronov zritel'noy kory krolika. Farmakologiya i toksikologiya (Moskva). 37(5):549-552, 1974.

The influence of microiontophoretic application of norepinephrine on spontaneous and photo induced electrical activity in the visual cortex neurons was investigated in rabbits. Norepinephrine was found to exert a strong and immediate inhibitory effect on the rabbits' visual neural activity. Norepinephrine elicited a hyperpolarization of the membrane of cortex neurons similar to the hyperpolarization of spinal neurons. It is therefore suggested that norepinephrine is a true inhibitor in the visual cortex. 21 references. (Journal abstract modified)

206542 Mandell, A. J.; Hsu, L. L. Department of Psychiatry, University of California at San Diego, La Jolla, CA **A two-factor biochemical theory of schizophrenia.** Totus Homo (Milano). 5(1-2-3):97-104, 1974.

Evidence that N-methylation of aromatic amines in brain may contribute to the onset of psychosis is reported. N-methylation of tryptamine and beta-phenylethylamine by purified enzyme fractions from rat brain, using S-adenosylmethionine (SAM) and 5-methyltetrahydrofolic acid (5-MTHF) as methyl donors were compared. There may be both a specific enzyme that can use either donor to methylate indoleamines and a nonspecific enzyme that can use either donor to methylate phenylethylamines and indoleamines. In addition, studies of neural responses to acute and chronic ad-

ministration of a variety of drugs and exogenous amines point to several discrete but related mechanisms by means of which the brain can compensate for disruptions in neural transmission, i.e. adaptations in receptor function, in enzyme conformation and activity, in substrate uptake, and in subcellular distribution of enzyme activity or amount. Psychotogenic compounds per se probably cannot cause long-term psychotic disorder without a failure of synaptic adaptive mechanisms (tolerance). (Author abstract modified)

206768 Sabelli, H. C.; Giardina, W. J.; Miles, S. B.; Vazquez, A. J. Dept. of Pharmacology, Chicago Medical School, 2020 W. Ogden Avenue, Chicago, IL 60612 **The effects of DOPA on the visual-evoked potentials in rabbit and on mouse motor behavior following inhibition of dopamine-beta-hydroxylase.** Arzneimittel-Forschung (Aulendorf). 24(3):333-337, 1974.

The effects of intravenous levo-dihydroxy-phenylalanine (DOPA) upon optic cortex potentials evoked by flash stimuli were studied on nonanesthetized rabbits. The fast (FPC) and slow (SNW) components of the averaged potential were analyzed for changes in amplitude. Findings suggest a SNW enhancing effect of low doses of DOPA which is attributable to the synthesis of dopamine (DA). The SNW depressing effect of higher doses of DOPA may depend on norepinephrine (NE) synthesis. Dopa depressed the locomotor exploratory behavior of single mice. Since neither FLA-63 nor tetraethylthiuram disulfide (TETD) prevented this depressant effect, it appears to be attributable to DA synthesis. In isocarboxazid treated mice, DOPA induced hostility and fighting in grouped mice. This stimulant effect was blocked by TETD pretreatment and may require NE synthesis. 24 references. (Author abstract modified)

206769 Scheele, G.; Weissenstein, H. 6 Frankfurt/Main 60, Gagernstr. 28, Germany **/Microautoradiographic studies after medication of C-14 labelled fluphenazine in the animal experiment./** Mikroautoradiographische Untersuchungen nach Medikation von mit C-14 markiertem Fluphenazin im Tierversuch. Arzneimittel-Forschung (Aulendorf). 24(3):326-330, 1974.

The distribution pattern and kinetics of C-14 labelled fluphenazine and C-14 labelled phenobarbital were investigated through microautoradiographic studies. Findings confirm values and results found by scintillation counts of isolated organ tissue and demonstrate the deposition of labelled fluphenazine in the nucleus of the stem ganglia. Distribution studies indicate that fluphenazine is accumulated more in the mesencephalon than in the anterior brain of the rabbit; phenobarbital, in comparison with fluphenazine, is accumulated less in the mesencephalon and more in the anterior brain. 5 references. (Author abstract modified)

206781 Ruberg-Schweer, M.; Karger, W. Institut fur Physiologie der Ruhr-Universitat, Arbeitsgruppe Physiologie der Membranen, 463 Bochum, Gebaude MA, Germany **/Influence of meprobamate, carisprodol, oxazepam and phenobarbital on Na+ transport in the isolated frog skin./** Beeinflussung des Na+-Transportes an der isolierten Forschhaut durch Meprobamat, Carisoprodol, Oxazepam und Phenobarbital. Arzneimittel-Forschung (Aulendorf). 24(10):1568-1574, 1974.

To clarify the interaction between neuroleptic drugs and biological membranes, the influence of several tranquilizers on the active transport of sodium ions in the isolated frog skin of Rana temporaria was investigated. Drugs included meprobamate, carisoprodol, oxazepam and phenobarbital. By measuring the changes of skin potential and short circuit current in their time course after drug application, it was shown that the corium side of the frog skin is preferentially sensitive for those drugs. Generally, skin potential and current values were reduced, indicating an interference between the ion transport mechanism and the drug in question. The most effective substance was oxazepam. This substance blocked sodium ion transport in the bath solution on the corium side. 72 references. (Author abstract modified)

206782 Shah, U. H.; Jindal, M. N.; Patel, V. K.; Kelkar, V. V. Dept. of Pharmacology, B. J. Medical College, Ahmedabad-16, Gujarat, India **Central actions of some beta-adrenoceptor blocking agents.** Arzneimittel-Forschung (Aulendorf). 24(10):1581-1584, 1974.

Central actions of several beta-adrenoceptor blocking agents were examined in mice and rats, with particular attention to their relative potencies. Drugs used were: pronethalol, propranolol, MJ-1999, USVC-6524, Inpea, dichlorisoproterenol (DCI), and practolol. Pronethalol, propranolol, MJ-1999 and USVC-6524 were active against maximal electroshock seizures (MES), while DCI, Inpea and practolol did not modify the MES pattern. Only propranol and USVC-6524 exhibited protection against metrazole. Propranolol and practolol afforded significant protection against strychnine toxicity. Propranolol, pronetholol, USVC-6524, MJ-1999 and practolol exhibited considerable antinicotinic activity, while propranolol, USVC-6524 and pronethalol afforded marked protection against amphetamine toxicity. All agents reduced the duration of sleep induced by pentobarbitone and ethanol in mice. Propranolol, pronetholol and USVC-6524 exhibited analgesic activity in rats. All agents reduced the analgesic activity of morphine. 28 references. (Author abstract modified)

206785 Merlo, L.; Noseda, V.; Ferrini, R.; Miragoli, G.; Marchetti, G. Instituto Simes di Cardiologia Sperimentale, Via Camillo Columbi, 18, I-20161, Milan, Italy **Effect of camazepam (SB-5833), a new antianxious drug, on cardiac contractility and coronary hemodynamics.** Arzneimittel-Forschung (Aulendorf). 24(11):1759-1762, 1974.

The effects of camazepam (SB-5833) on cardiac contractility and hemodynamics were tested both in vitro and in conscious dogs and compared with effects of compounds having similar antianxiety activity. In vitro investigations demonstrated that camazepam has a slight positive inotropic effect, whereas chlordiazepoxide, temazepam, diazepam and medazepam reduce cardiac contractility. In conscious dogs, camazepam given intravenously had no effect on the cardiac function, while chlordiazepoxide and temazepam reduce aortic and ventricular pressure and time course of the pressure change. 12 references. (Author abstract modified)

206809 Fischer, E.; Heller, B. Hospital Nacional, Barracas 375, Buenos Aires, Argentina **Methyl-amphetamine and phenethylamine.** Arzneimittel-Forschung (Aulendorf). 24(6):956, 1974.

The effect of methylamphetamine on brain phenethylamine was studied in rats. Concentration of brain phenethylamine was diminished after prolonged treatment. The original value of 0.5micrograms/g rat brain was lowered to 0.05 micrograms/g after 21 days of daily intraparenteral injections of 5mg/kg of methylamphetamine. Phenethylamine is considered a brain neurohumoral agent of stimulating (ergotropic) character, and it is suggested that amphetamine acts centrally by liberating phenethylamine. 4 references. (Author abstract)

206912 Saunders, D. R.; Paolino, R. M.; Bousquet, W. F.; Miya, T. S. Department of Pharmacology-Toxicology, School of Pharmacy and Pharmacal Science, Purdue University, Lafayette, Indiana 47907 **Age-related responsiveness of the rat to drugs affecting the central nervous system.** Proceedings of the Society for Experimental Biology and Medicine. 147(3):593-595, 1974.

Age related alterations in the responsiveness of mature rats to centrally acting drugs were investigated, emphasizing the importance of regarding the age of the animal as a significant factor in assessing drug response. Responses to sodium hexobarbital, chlorpromazine HCl, morphine SO4, and d-amphetamine SO4 were evaluated in 2.5-3-month-old and 9-10-month-old male rats. Differences in responsiveness to the drugs was evident between the age groups. Several mechanisms are probably involved in this phenomenon, including alterations in drug distribution, metabolism, elimination and target organ sensitivity. In pharmacologic studies, age of the animals should be considered as one of the experimental variables to be controlled and reported. 6 references.

206913 Oldendorf, William H. Research and Neurology Services, Wadsworth Hospital Center, Veterans Administration, Los Angeles, CA 90073 **Lipid solubility and drug penetration of the blood brain barrier.** Proceedings of the Society for Experimental Biology and Medicine. 147(3):813-816, 1974.

The relationship between lipid solubility and drug penetration of the blood - brain barrier was examined by using lipid/water partition coefficients of 19 radiolabeled drugs which were correlated with uptake by brain during a single microcirculatory passage following carotid arterial injection. Uptake was measured relative to a simultaneously injected diffusible reference. When the lipid/water partition coefficient was greater than about 0.03 a substantial fraction of the drug penetrated the blood - brain barrier. For most drugs above this range, uptake was essentially complete. Findings suggest there is probably little reason to greatly exceed this degree of lipid solubility when designing drugs for blood - brain barrier penetration and central nervous system effects. 15 references.

206972 Sayers, A. C.; Kleinlogel, H. Forschungsinstitut Wander AG, Sandoz-Forschungsgruppe, Bern, Switzerland **/Neuropharmacological findings after chronic administration of haloperidol, loxapine and clozapine./** Neuropharmakologische Befunde unter chronischer Verabreichung von Haloperidol, Loxapin und Clozapin. Arzneimittel-Forschung (Aulendorf). 24(7):981-983, 1974.

Neuropharmacological findings in rats are reported after chronic administration of haloperidol, loxapine and the new antipsychotic drug, clozapine. All three agents exerted similar effects on the electroencephalographic sleep pattern. Dozing was increased and qualitatively altered, while waking time, slow wave sleep and paradoxical sleep were reduced. These changes persisted during chronic administration of the compounds over a 28 day period. No rebound occurred on termination of treatment. The three compounds also potentiated evoked caudate spindles in rats. Tolerance to this effect developed after haloperidol and loxapine but not after clozapine. A possible correlation between these findings and an antipsychotic action is briefly discussed. 7 references. (Author abstract modified)

206973 Burki, H. R. Forschungsinstitut Wander AG, Sandoz-Forschungsgruppe, Bern, Switzerland **/Metabolism of dopamine and norepinephrine in rat brain after single and repeated administration of haloperidol, loxapine and clozapine./** Metabolismus von Dopamin und Noradrenalin im Hirn der Ratte nach akuter und chronischer Verabreichung von Haloperidol, Loxapin und Clozapin. Arzneimittel-Forschung (Aulendorf). 24(7):983-984, 1974.

Metabolism of dopamine and norepinephrine was investigated in the rat brain after administration of two neuroleptics, and a pronounced activation of the dopaminergic neurons of the neostriatum was found after a single administration of haloperidol and loxapine. The dopamine (DA) turnover was increased, the DA content was reduced and the content of the DA metabolite homovanillic acid (HVA) was strongly elevated over several hours. These effects appear to be related to the cataleptogenic and antiapomorphine actions of these drugs and seem to result from a blockade of striatal DA receptors, thus initiating a feedback stimulation of dopaminergic neurons. After repeated administration of these drugs, tolerance developed to these effects and cross tolerance between haloperidol and loxapine was observed with respect to the increase in striatal HVA. Clozapine caused an increase in striatal HVA only at high doses, and no tolerance developed to the increase in HVA after repeated administration. After multiple dosage, however, an increase in the striatal DA content was observed, an effect not seen with neuroleptic drugs. 26 references. (Author abstract modified)

206988 Blasig, J.; Papeschi, R.; Herz, A. Max-Planck-Institut fur Psychiatrie, 8 Munchen 40, Kraepelinstr. 2, Germany **/Significance of catecholamines for the manifestation of morphine withdrawal in the rat./** Bedeutung der Katecholamine bei der Manifestation des Morphinentzugs bei der Ratte. Arzneimittel-Forschung (Aulendorf). 24(7):1015-1016, 1974.

The role of catecholaminergic mechanisms in the expression of morphine withdrawal was investigated in rats. Quantification of precipitated withdrawal was based on a previous study in which a series of signs were qualitatively evaluated. The severity of withdrawal was aggravated by pretreatment with drugs which increase catecholaminergic activity such as L-dopa, d-amphetamine, apomorphine and desipramine. On the other hand, pretreatment with alpha-methyl-p-tyrosine (AMT) or FLA-63 decreased with intensity of withdrawal. The effect of AMT was reversed by L-dopa but only incompletely antagonized by apomorphine or a combined FLA-63 and L-dopa treatment. Results indicate that catecholamines, dopamine and noradrenaline play an important role in the expression of the withdrawal syndrome. 9 references. (Author abstract modified)

206989 Papeschi, R.; Theiss, P.; Herz, A. Abteilung fur Neuropharmakologie, Max-Planck-Institut fur Psychiatrie, 8 Munchen, Kraepelinstr. 2, Germany **Serotonin and dopamine turnover after acute and chronic morphine administration.** Arzneimittel-Forschung (Aulendorf). 24(7):1017-1019, 1974.

A neurochemical investigation of the effects of chronic morphine administration is reported in which the preliminary administration of morphine increased the accumulation of homovanillic acid (HVA) in the rat brain after probenecid, even after the smallest (10mg/kg) dose of morphine tested. The accumulation of 5-hydroxyindoleacetic acid (5-HIAA) was only increased after 40mg/kg. The preliminary chronic subcutaneous implantation with morphine pellets over different periods of time and with different implantation frequencies also increased the accumulation of both HVA and 5-HIAA after probenecid; however, no marked differences were noticed in this effect in the various groups of rats according to degree of morphine tolerance/dependence. The group with highest tolerance/dependence showed no difference from the controls in the accumulation of 5-HIAA at the longest interval

after probenecid. Results are discussed in relation to the acute neurochemical effects of morphine and the influence of increased dopaminergic and serotonergic turnovers on the development of morphine tolerance/dependence. 12 references. (Author abstract modified)

206990 Karobath, Manfred. Psychiatrische Universitatsklinik, Lazarettgasse 14, A-1090, Vienna, Austria **/Tricyclic antidepressant drugs and dopamine sensitive adenylcyclase from rat caudate nuclei./** Trizyklische antidepressive Substanzen und dopamin-sensitive Adenylcyclase aus dem Nucleus caudatus der Ratte. Arzneimittel-Forschung (Aulendorf). 24(7):1019-1021, 1974.

The effects of tricyclic antidepressant drugs in caudate nuclei of rats were investigated to determine their actions as inhibitors of dopamine stimulated adenylate cyclase. Imipramine, desimipramine and nortriptyline showed minor inhibitory effects; but the stimulation by dopamine was considerably decreased by amitriptyline. A similar effect was seen with chlorpromazine. 11 references. (Author abstract modified)

206993 Ladisich, W. Max-Planck-Gesellschaft, 8 Munchen 40, Kraepelinstr. 10, Germany **/Effect of stress upon serotonin metabolism in various regions of the rat brain./** Stress und Serotoninstoffwechsel in verschiedenen Arealen des Zentralnervensystems der Ratte. Arzneimittel-Forschung (Aulendorf). 24(7):1025-1027, 1974.

The effect of stress upon serotonin metabolism in the rat brain was investigated, and electric footshock resulted in a considerable increase of 5-hydroxyindoleacetic acid (5-HIAA) and serotonin (5-HT) concentrations. The increase of 5-HIAA was most pronounced in septum and raphe, while 5-HT concentrations rose mainly in septum, thalamus and hypothalamus. Monoamine oxidase (MAO) inhibition did not appear to be a good indicator for studying 5-HT turnover. A certain analgetic effect due to MAO inhibition was thought to change the hierachy of different reactions in the brain areas investigated. In general, however, septum and raphe appeared to be the regions whose 5-HT metabolism was most effected by the stress of footshock. There were no significant results in any brain region in a study of the effect of an approach - avoidance conflict upon 5-HT metabolism. 9 references. (Author abstract modified)

206997 Hoefke, W.; Warnke-Sachs, E. 6507 Ingelheim, Fa. C. H. Boehringer Sohn, Abt. Pharmaforschung-Biologie, Germany **Influence of desmethylimipramine on the hypotensive effect of clonidine.** Arzneimittel-Forschung (Aulendorf). 24(7):1046-1047, 1974.

The influence of desmethylimipramine on the hypotensive effect of clonidine was studied in anesthetized rabbits. The hypotensive effect of clonidine was not diminished by acute pretreatment with desmethylimipramine. 10 references. (Author abstract modified)

207198 Polezhaeva, A. I.; Sinyukhin, V. N. Laboratoriya farmakologii, Vsesoyuzhogo nauchnoissledovatel'skogo khimiko - farmatsevticheskogo instituta im. S. Ordzhonikidze, Moscow **/On the pharmacology of desmethyl azaphen derivatives./** K farmakologii desmetil'nykh proizvodnykh azafena. Farmakologiya i Toksikologiya (Moskva). 37(1):8-10, 1974.

A comparative pharmacological analysis of azaphen and its desmethyl derivatives was carried out on white mice. Monodesmethyl and didesmethyl derivatives were found to be closely related to azaphen. Like azaphen, its derivatives strengthened hyperthermic activity and the group toxicity of fenamine, and weakened the effects of reserpine and tetrabenazine. Both the monodesmethyl and didesmethyl derivatives were found to be less toxic than azaphen, although the strength of didesmethyl activity was equal to and sometimes stronger than that of azaphen. 9 references. (Journal abstract modified)

207199 Vikhlyaev, Yu. I.; Lando, L. I.; Segal, A. M. no address **/The effect of diazepam and nitrazepam on intracellular and extracellular distribution of sodium and potassium ions in individual structures of rats' brains./** Vliyaniye diazepama i nitrazepama na vnutri- i vnekletochnoye raspredeleniye ionov natriya i kaliya v otdel'nykh strukturakh golovnogo mozga krys. Farmakologiya i Toksikologiya (Moscow). 37(1):10-14, 1974.

The influence of diazepam and nitrazepam on intracellular and extracellular distribution of sodium and potassium ions in the temporal cortex, hippocampus and remaining section of the brain was studied in albino rats. Diazepam and nitrazepam were found to effect similar changes in the ionic composition of the brain. Diazepam and nitrazepam raised the proportion of sodium ions in the brain, at the expense of a lowering of sodium's intracellular concentration. Large doses of both substances raised the potassium gradient in the temporal cortex, hippocampus and remaining brain, at the expense of a lowering of extracellular potassium concentration. In all cases, the most extensive changes occurred in the hippocampus, and the lesser ones in the temporal cortex and remaining brain. 16 references. (Journal abstract modified)

207200 Kryzhanovskiy, G. N.; Sheykhon, F. D.; Igon'kina, S. I. Laboratoriya patologii infektsionnykh intoksikatsiy, Instituta normal'noy i patologicheskoy fiziologii, Moscow **/The effect of L-DOPA and L-DOPA combined with chlorpromazine on spinal cord activity during disturbed inhibition by tetanus toxoid./** Vliyaniye L-DOFA i L-DOFA v sochetanii s aminazinom na aktivnost' spinnogo mozga v usloviyakh narusheniya tormozheniya stolbnyachnym toksinom. Farmakologiya i Toksikologiya (Moscow). 37(1):21-25, 1974.

The effect of L-DOPA and chlorpromazine on reflex reactions of the spinal cord under the localized influence of tetanus toxoid was studied in albino rats. Intravenous injections of L-DOPA in 50-100 mg doses was found to exert a two phase influence on the spinal cord: inhibition of background activity during the first 10 to 20 minutes; and a subsequent increase in the reflex activity of the affected parts of the spinal cord during the next 1 to 2 hours. The simultaneous action of L-DOPA and chlorpromazine in doses of 75 mg/kg produced a prolonged inhibition stage, with no subsequent increase in reflex activity. 25 references. (Journal abstract modified)

207283 Fleischhauer, J.; Al-Shaltchi, B.; Brandli, A. Psychiatrische Universitatsklinik Wilhelm-Klein-Strasse 27, CH-4025, Basel, Switzerland **/Report on a preliminary clinical study of mianserin (GB 94), a tetracyclic antidepressant, an open trial./** Bericht uber eine erste klinische Prufung von Mianserin (GB 94), einem tetrazyklischen Antidepressivum, im offenen Versuch. Arzneimittel-Forschung (Aulendorf). 23(12):1808-1813, 1973.

The results of an open clinical study with a new tetracyclic antidepressant drug, mianserin (GB-94), are reported. Findings reveal that the drug is effective as an antidepressant, and that there are no anticholinergic side effects. Aside from its mood elevating effect, the drug produces slight sedation and shows good efficiency against anxiety. No metabolic influence on

biogenic amines in the central nervous system was found with the exception of an influence on dopamine. 12 references. (Author abstract modified)

207288 Baldessarini, Ross J.; Harris, Jane E. Psychiatric Research Laboratories, Massachusetts General Hospital, Boston, MA 02114 **Effects of amphetamines on the metabolism of catecholamines in the rat brain.** Journal of Psychiatric Research (Oxford). 11:41-43, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the uptake of (3H)DA elucidated by a synaptosomal preparation of the rat corpus striatum was discussed. The inhibitory concentration required to produce a 50% reduction of the accumulation of 0.1micromolar (3H)DA for the (+)-isomer of amphetamine was about four times less than for the (-)-isomer in inhibiting the net accumulation of DA. With cortical homogenates, the dextrorotatory isomer of amphetamine was only slightly more potent in inhibiting the uptake of NE and DA than the (-)-enantiomer. Findings in the striatal synaptosomes from rats which had not been pretreated with drugs correspond closely to their different potencies in producing stereotyped behavior in the rat. 9 references.

207290 Carlsson, Arvid. Department of Pharmacology, University of Gotegorg, Goteborg, Sweden **Antipsychotic drugs and catecholamine synapses.** Journal of Psychiatric Research (Oxford). 11:57-64, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the role of neuroleptics in interfering with catecholamine neurotransmission in the brain was discussed. Reserpine causes depletion of monoamine stores, thereby reducing the amounts of monoamine transmitters available for release by the nerve impulses. If both reserpine and its competitor disappear rapidly from body fluids, and if the binding of the competitor is entirely reversible, normal physiological conditions are restored, because the irreversible binding of reserpine has been prevented. The antipsychotic action of neuroleptic drugs is brought about by reducing the activity of central catecholamine receptors. Dopamine receptors seem more specifically involved in this action than noradrenaline receptors which, however, may play a contributory role. 21 references.

207294 Bunney, B. S. no address **Dopaminergic blocking effects of antipsychotic drugs.** Journal of Psychiatric Research (Oxford). 11:72-73, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, extracellular single unit recording technique findings in rats on the effect of drugs on the firing rate of dopaminergic neurons in the substantia nigra - zona compacta and ventral tegmental areas are reported. D-amphetamine in small doses depressed dopamine cell activity. The antipsychotic phenothiazines and haloperidol both block and reverse this depressant effect. A histogram representing the activity of a single dopamine cell is included for several rats. Findings suggest that dopamine receptors may be present on the dopamine cell body itself.

207296 Glowinski, Jacques. Laboratory of General Neurophysiology, Biochemical Neuropharmacology Unit, College de France, Paris, France **New developments in the study of the mechanism of action of neuroleptics and amphetamine.** Journal of Psychiatric Research (Oxford). 11:81-85, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the mechanism of action of neuroleptics and amphetamines was discussed relative to their effects on central aminergic neurones. Dopaminergic terminals have been found in the cerebral cortex of the rat which had not been previously observed in histochemical studies. Neuroleptics or amphetamine and its derivatives could act on the cortical dopaminergic system as well as upon other noradrenergic or dopaminergic systems. Repeated daily injections of thioproperazine, a neuroleptic of the phenothiazine type, significantly decrease the baseline activity of the nigro neostriatal dopaminergic pathway in the rat. 23 references.

207297 Greengard, Paul. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Biochemical characterization of the dopamine receptor in the mammalian caudate nucleus.** Journal of Psychiatric Research (Oxford). 11:87-90, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the dopamine receptor of the caudate nucleus was discussed, considering that this dopamine receptor might, like the dopamine receptor in the ganglion, be the dopamine binding portion of a dopamine sensitive adenylate cyclase activity. Such an adenylate cyclase was found in the caudate nucleus, and interestingly, virtually all of the known properties of the caudate dopamine receptor could be mimicked by the properties of this cell free enzyme system. Characteristics such as a mild sensitivity to inhibition by alpha-adrenergic blocking agents, and a total insensitivity to inhibition by beta-adrenergic blocking agents, provided further evidence for the possible identity of the dopamine sensitive adenylate cyclase and the dopamine receptor. It should now be possible to search for new anti-Parkinson agents by testing compounds for their ability to stimulate dopamine sensitive adenylate cylase of the caudate nucleus. 4 references.

207298 Snyder, Solomon H.; Greenberg, David; Yamumura, Henry I. Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Antischizophrenic drugs: affinity for muscarinic cholinergic receptor sites in the brain predicts extrapyramidal effects.** Journal of Psychiatric Research (Oxford). 11:91-95, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, antischizophrenic drugs and their affinity for muscarinic cholinergic receptor sites were examined as predictors in extrapyramidal effects in the brain. Butyrophenone drugs such as haloperidol and piperazine phenothiazines and perphenazine produce considerably more extrapyramidal effects than alkylamino phenothiazines. An alternative explanation for variations in the incidence of extrapyramidal effects lies in the anticholinergic actions of phenothiazines. By blocking muscarinic cholinergic receptors in the brain, phenothiazines might antagonize their own tendency to elicit extrapyramidal symptoms via dopamine receptor blockade. Using a simple, sensitive and specific assay for the muscarinic cholinergic receptor in the brain, the relative affinities for a variety of antischizophrenic drugs were evaluated. The apparent balance of cholinergic and dopaminergic mechanisms in producing extrapyramidal symptoms is presumed to operate in the corpus striatum. Therapeutic antischizophrenic dopamine receptor blockade requires almost ten times higher brain levels of thioridazine than of trifluoperazine. 14 references.

207299 Anden, Nils-Erik. Department of Pharmacology, University of Goteborg, Goteborg, Sweden **Antipsychotic drugs and catecholamine synapses: summary of the session.** Journal of Psychiatric Research (Oxford). 11:97-104, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the effects of the neuroleptic drugs on the central catecholamines were discussed. The dopamine neurotransmission is inhibited by all the neuroleptic drugs tested, the phenothiazines and the butyrophenones, by a blockade of the postsynaptic receptors. Most also interfered with central noradrenaline mechanisms. A blockade of central catecholamine receptors results in a compensatory increase in the synthesis and release of the catecholamine of the presynaptic neuron. The extrapyramidal and antipsychotic actions may be evoked by a reduced dopamine receptor activity in the corpus striatum and in the limbic system, respectively. 34 references. (Author abstract modified)

207300 Matthysse, S. Psychiatric Research Laboratories, Massachusetts General Hospital, Boston, MA **Dopamine and the pharmacology of schizophrenia: the state of the evidence.** Journal of Psychiatric Research (Oxford). 11:107-113, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the connection between dopamine and schizophrenia was examined. The blocking effects of antipsychotic drugs on amphetamine and apomorphine induced stereotyped behavior, the approximate equality of potency of d-amphetamine and l-amphetamine in eliciting psychosis, and the ability of the antipsychotics to enhance brain dopamine turnover were discussed as primary evidence connecting dopamine transmission with schizophrenia. The evidence is favorable to a "dopamine hypothesis", but there are contradictions in stereotypy blockade, in the comparison of d-amphetamine and l-amphetamine, and in the dopamine turnover enhancing effects of tranquilizing drugs. 22 references.

207304 Ungerstedt, Urban; Ljungberg, Tomas. Department of Histology, Karolinska Institutet, Stockholm, Sweden **Central dopamine neurons and sensory processing.** Journal of Psychiatric Research (Oxford). 11:149-150, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the relation of central dopamine (DA) neurons' hypofunction to decreased sensory awareness or responses is examined. DA hypofunction may be important in relation to neuroleptic therapy for schizophrenia. If schizophrenia primarily is a disturbance in DA function, the neuroleptic drugs interfere with the disease process itself. However, if the true disturbance is somewhere else, the effectiveness of these drugs may only depend upon the fact that they interfere with processes directly related to the "carrying out" of behavior and thus are eminently suited to cover up any existing mental disturbance and prevent it from showing up in behavior. 7 references.

207305 Fuxe, K.; Nystrom, M.; Tovi, M.; Smith, R.; Ogren, S.-O. Department of Histology, Karolinska Institutet, 104 01 Stockholm, Sweden **Central catecholamine neurons, behavior and neuroleptic drugs: an analysis to understand the involvement of catecholamines in schizophrenia.** Journal of Psychiatric Research (Oxford). 11:151-161, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the role of catecholamine (CA) neurons in unconditioned locomotor behavior, reward behavior, and conditioned avoidance behavior was discussed. Stereotyped behavior seems to be mainly related to DA receptor activation. The NA pathways, especially the cortical pathways, are involved in learning. Endocrine factors strongly influence these NA pathways, and loss of the NA cortical pathways can be compensated for provided that adrenocortical steroids are present. A "biochemical lesion" in a catecholamine pathway together with a hormonal disturbance may result in a "schizophrenic brain" where compensation no longer can occur, resulting in a permanent impairment of mental function. 46 references.

207307 Mandell, Arnold J. Department of Psychiatry, University of California, San Diego, La Jolla, CA 92037 **The role of adaptive regulation in the pathophysiology of psychiatric disease.** Journal of Psychiatric Research (Oxford). 11:173-179, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, five processes in central synapses of the dopaminergic, noradrenergic, and serotonergic systems were discussed. Pharmacological manipulations that chronically deplete the levels of catecholamines in the synapse apparently result in potentiated receptor sensitivity to the neurotransmitter. Alterations in enzyme conformation and activity, alterations in substrate uptake, delayed alterations in enzyme amount or activity, and the axoplasmic flow rates of enzymes were reported. Results indicate that the brain is vulnerable to the consequences of failures in regulation and adaptation. Normally, when a regulatory component fails or a genetic deficiency prevails, other brain mechanisms respond to compensate for the disruption. The adaptive mechanisms are the major impediment to any continuing role in mental disorder for an aberrant metabolite. 17 references.

207326 Thomas, James A.; Van Orden, L. S., III; Redick, J. A.; Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Immunological localization of dopamine-beta-hydroxylase on the chromaffin granule membrane.** Journal of Psychiatric Research (Oxford). 11:317-319, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the effect of antibodies to bovine dopamine-beta-hydroxylase (DBH) on the activity of the enzyme in lysed and intact bovine medullary granules was examined. Incubation of lysed granules with anti-DBH serum resulted in about 80% inhibition of the enzyme. A portion of the antigenic sites of DBH were concluded to be located on the exterior of the vesicular membrane. The DBH activity of intact vesicles is only about half that of the total activity. 7 references.

207333 Bhagat, B.; Misra, C. H. no address **Possible role of catecholamines (CA) in the regulation of adrenal tyrosine hydroxylase (TH).** Journal of Psychiatric Research (Oxford). 11:361, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the hypothesis that the depletion of adrenal CA may have a role in an induction of adrenal tyrosine hydroxylase (TH) was examined. The decreased receptor response and the consequent hypotension after alpha-adrenergic blockade results in a stimulation of adrenergic nerve activity to maintain homeostasis. The alpha-blocking drug phentolamine which did not reduce adrenal catecholamine

content failed to elicit an increase in adrenal TH activity. Thus, in addition to increased nerve activity, depletion of catecholamines is a prerequisite for induction of adrenal TH.

207500 Cheney, D. L.; Racagni, G.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **The effect of clozapine and acetylcholine turnover rate in rat striatum. (Unpublished paper).** Bethesda, MD, NIMH, 1975. 1 p.

To study the effect of clozapine and acetylcholine (ACh) in rat striatum, rats were killed in 2 seconds with focused microwave radiation and turnover rate of ACh was measured. Both clozapine and haloperidol blocked the stimulation of striatal adenyl cyclase by dopamine and reverse the decreased striatal ACh turnover rate elicited by apomorphine. Clozapine decrease the striatal content of ACh but did not alter the turnover rate of ACh; haloperidol failed to reduce the striatal ACh content but increase the ACh turnover in striatum. Thus clozapine, but not haloperidol, mimicked the action of the anticholinergic drugs artane and benztropine on striatal ACh. These drugs and clozapine antagonized the increased striatal ACh content and the decreased ACh turnover rate elicited by arecoline and oxotremorine. It appears that clozapine shares with the neuroleptics the ability to block striatal dopamine receptors, and with the anticholinergics the ability to block the striatal ACh receptors. (Author abstract modified)

207798 Mao, C. C.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC 20032 **Inhibition by diazepam of the tremor and the increase of cerebellar cGMP content elicited by harmaline.** Brain Research (Amsterdam). 83(3):516-519, 1975.

Inhibition by diazepam of the tremor and increase of cerebellar 3′5′-cyclic guanosine monophosphate (cGMP) content elicited by harmaline was examined. Male Sprague-Dawley rats about 150g in bodyweight were killed by high intensity microwave beam. Data suggest that the cGMP system is involved in the action of harmaline on cerebellum and that diazepam, an anticonvulsant, antagonizes the tremorogenic effect of harmaline and the increase of cerebellar cGMP elicited by harmaline. It is noted that the cGMP concentration is drastically reduced in mice with a genetic degeneration of Purkinje cells and that the cerebellar cGMP content of these mice is not reduced by diazepam. It is then inferred that the Purkinje cells may be a site of action for diazepam in cerebellum and that the burst discharges of Purkinje cells elicited by the climbing fiber activation caused by harmaline may be blocked by diazepam. 12 references.

207857 Abeles, Robert H.; Tashjian, Armen H., Jr. Graduate Dept. of Biochemistry, Brandeis Univ., Waltham, MA 02154 **Comparison of the inhibitory effects of propargylamine and pargyline on brain and liver monoamone oxidase activity.** Biochemical Pharmacology (Oxford). 24(2):307-308, 1975.

A comparison of the inhibitory effects of propargylamine and pargyline on brain and liver monoamine oxidase activity in the mouse is reported. Results show that propargylamine and pargyline are equally effective in inhibiting monoamine oxidase (MAO) activity in the mouse liver and in brain. At a given dose level, the liver enzyme was inhibited to a greater extent than brain MAO. Liver MAO activity returned fully to the control level by the seventh day after a single dose of inhibitor while the brain enzyme showed no appreciable recovery in the period or after 21 days. The inhibitory effects of propargylamine and pargyline in vivo on both liver and brain MAO are consistent with the mechanism proposed from studies in vitro. The prolonged inhibitory effects observed confirm other results which suggest that the brain enzyme is renewed at a rate which is slower than that of liver MAO. 7 references.

208300 Forn, Javier; Krueger, Bruce K.; Greengard, Paul. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Adenosine 3′,5′-monophosphate content in rat caudate nucleus: demonstration of dopaminergic and adrenergic receptors.** Science. 186(4169):1118-1120, 1974.

The effects of dopamine and other catecholamines on the content of adenosine 3′,5′-cyclic monophosphate (cyclic-AMP) in slices of rat caudate nucleus were examined. Dopamine, apomorphine, isoproterenol and norepinephrine each increased the concentration of cyclic-AMP in slices of rat caudate nucleus. The concentrations of dopamine, apomorphine, isoproterenol, and norepinephrine causing half-maximal increases are reported. The effect of dopamine was blocked by fluphenazine, a dopamine receptor antagonist, but not by propranolol, a beta-adrenergic receptor antagonist. Conversely, the effect of isoproterenol was blocked by propranolol but not by fluphenazine. The results suggest that in rat caudate nucleus there are two distinct catecholamine receptors capable of causing increased concentrations of cyclic-AMP, one having the characteristics of a dopamine receptor, and the other having the characteristics of a beta-adrenergic receptor. 21 references. (Author abstract modified)

208552 Thornburg, J. E.; Moore, K. E. Dept. of Pharmacology, Michigan State University, East Lansing, MI 48824 **Supersensitivity to dopamine agonists following unilateral, 6-hydroxydopamine-induced striatal lesions in mice.** Journal of Pharmacology and Experimental Therapeutics. 192(1):42-49, 1975.

The sensitivity of postsynaptic dopaminergic receptors in the lesioned striatum was studied. Mice were injected with 6-hydroxydopamine in the left striatum. Mice initially circled spontaneously in the direction of the lesion and gradually developed an ability to circle in the opposite direction when challenged with apomophine and L-dopa. Dose response curves for apormophine and L-dopa induced circling rates shifted to the left as the duration between the time of the 6-hydroxydopamine injection and the time of testing increased from two to 30 days. There was a positive correlation between the rate of apomorphine induced circling and the reduction in the dopamine concentration in the lesioned forebrain. Doses of apomorphine and L-dopa required to elicit circling responses were one sixth to one tenth of those required to increase locomotor activity in mice. Data support the concept of development of supersensitivity of postsynaptic dopaminergic receptors in the lesioned striatum. 27 references. (Author abstract modified)

208553 Sanders-Bush, E.; Bushing, J. A.; Sulser, F. Tennessee Neuropsychiatric Institute, Central State Hospital, Nashville, TN 37217 **Long-term effects of p-chloroamphetamine and related drugs on central serotonergic mechanisms.** Journal of Pharmacology and Experimental Therapeutics. 192(1):33-41, 1975.

The mechanism responsible for the long-term effects of p-chloroamph (PCA) and related drugs on central serotonergic mechanisms was studied. PCA was found to cause long lasting reductions in the level of serotonin (5-hydroxytryptamine; 5-HT) and the activity of tryptophan hydroxylase in brain, whereas the effects of fenfluramine disappeared two weeks

after injection. The effects on catecholamine uptake disappeared within one day after injection. In contrast, the time course of recovery of the synaptosomal uptake capacity for 5-HT followed a pattern similar to that found for the recovery level of 5-HT and the activity of tryptophan hydroxylase. The greatest reductions of 5-HT, tryptophan hydroxylase activity and synaptosomal uptake were found in the midbrain, hippocampus and striatum. Results indicate that different independent mechanisms are responsible for the initial reversible and the prolonged irreversible effects of PCA on serotonergic neurons. 31 references. (Author abstract modified)

208554 Eidelberg, E.; Erspamer, R. Barrow Neurological Institute, 350 W. Thomas Rd., Phoenix, AZ 85013 **Dopaminergic mechanisms of opiate actions in brain.** Journal of Pharmacology and Experimental Therapeutics. 192(1):50-57, 1975.

The interactions between morphine and a dopamine blocking agent (haloperidol) and a dopamine precursor, L-3,4-dihydroxyphenylalanine (L-dopa) were studied. It was found that haloperidol potentiated morphine induced analgesia and enhanced morphine tolerance. Morphine tolerant mice exhibited enhanced sensitivity to the locomotor excitatory actions of L-dopa. It is proposed that morphine exerts some of its central nervous actions by first interfering with dopamine mediated synaptic transmission and then initiating compensatory changes that superficially resemble denervation supersensitivity. These compensatory changes may underlie the excitatory actions of morphine. 52 references. (Author abstract modified)

208555 Russell, Roger W.; Overstreet, David H.; Cotman, Carl W.; Carson, Virginia G.; Churchill, Lynn; Dalglish, Frank W.; Vasquez, Beatriz J. School of Biological Sciences, Flinders University, Bedford Park, South Australia 5042 **Experimental tests of hypotheses about neurochemical mechanisms underlying behavioral tolerance to the anticholinesterase, diisopropyl fluorophosphate.** Journal of Pharmacology and Experimental Therapeutics. 192(1):73-85, 1975.

Neurochemical and psychopharmacological studies of rats were design examine four hypotheses which have been proposed to account for the development of behavioral tolerance to the anticholinesterase, diisopropyl fluorophosphate (DFP). Pilocarpine was less effective in suppressing the responding of rats tolerant to DFP than that of control subjects, confirming other evidence indicating that a decreased sensitivity of cholinergic (muscarinic) receptors is one mechanism underlying the development of tolerance to DFP. Findings relating to the three other hypotheses: 1) suggest that nonspecific metabolic changes are unlikely mechanisms of behavioral tolerance; 2) offer no support for the hypothesis that a redundant adrenergic system may replace the cholinergic system during the development of tolerance to DFP; and 3) tend to eliminate end product inhibition of acetylcholine synthesis as a primary mechanism of tolerance. 78 references. (Author abstract modified)

208636 Zivkovic, B.; Guidotti, A.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Are autoreceptors in dopaminergic neurons involved in the change of the kinetic state of striatal tyrosine hydroxylase elicited by antipsychotics? (Unpublished paper).** Washington, DC, NIMH, 1975. 1 p.

Antipsychotics of various classes were injected into rats and were shown to decrease the apparent Km of striatal tyrosine hydroxylase (TH) for pteridine cofactor. This change of the kinetic state of striatal TH was reversed by injections of apomorphine or piribedil, which failed to affect the kinetic state of striatal TH. Cerebral hemisection also changed the kinetic state of striatal TH; this change was maximal at 5 minutes and lasted for about 30 minutes. However, this change was not reversed by apomorphine. Moreover, haloperidol did not affect the kinetic state of striatal TH when given 30 minutes after cerebral hemisection. In rats treated with haloperidol, cerebral hemisection reversed the kinetic state of striatal TH within 30 minutes. These results demonstrate that the postsynaptic dopamine receptors and striatonigral neuronal loop that regulate the activity of dopaminergic neurons in substantia nigra are involved in regulating the change of the kinetic state of striatal TH induced by antipsychotics. (Author abstract modified)

208735 Costa, E.; Lehne, R.; Gnegy, M.; Uzunov, P. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **On the regulation of cyclic 3′,5′-AMP phosphodiesterase by a specific protein activator. (Unpublished paper).** Washington, DC, NIMH, 1975. 1 p.

Regulation of cyclic 3′,5′-adenosine monophosphate (AMP) phosphodie (PDE) by a specific protein activator was studied. PDE activator was isolated from rat brain, pineal gland, adrenal medulla and bullfrog sympathetic ganglia. In the presence of Ca++ the endogenous activator stimulated activator deficient PDE in a concentration dependent fashion. The activator was found to lack both tissue and species specificity. It activated PDE by reducing Km for cyclic 3,5-AMP and had no effect on Vmax. An in vivo increase of PDE activator was observed in rat adrenal medulla following injections of carbamylcholine or reserpine and cold exposure; analgous changes were found in pineal gland following reserpine injections. The effect was preceded by an increase in cyclic-AMP concentration. In vivo data suggest that the increase in cyclic-AMP tissue concentration may regulate the amount of PDE activator. (Author abstract modified)

208971 Il'yuchenok, R. Yu,; Martynov, N. N. Laboratoriya neyrofiziologii i farmakologii povedeniya, Instituta riziologii Sibirskigo otdeleniya AN SSSR, Novosibirsk, U.S.S.R. /**The role of dopamine and norepinephrine in changing the direct cortical response to phenamine.**/ Rol' dofamina i noradrenalina v izmenenii pryamogo korkovogo otveta pri deystvii fenamina. Farmakologiya i Toksikologiya (Moskva). 37(6):655-658, 1974.

The influence of dopamine and norepinephrine on changes in direct cortical response (DCR) induced by phenamine was studied on curarized nonanesthetized cats. Phenamine activity alone was found to depress the amplitude of direct cortical responses. With disulfiram blocking of dopamine-beta-hydroxylase, the systemic and topical use of phenamine produced a rise in DCR amplitude similar to that produced under application of a dopamine solution to the brain cortex of intact cats. Following a block of dopamine and norepinephrine synthesis with alpha-methyl-dopamine, the local systemic use of phenamine caused no material changes in the DCR. 15 references. (Journal abstract modified)

208972 Krauz, V. A. Laboratoriya eksperimental'noy farmakoterapii, otdela farmakologii, Instituta eksperimental'noy meditsiny AMN SSSR, Leningrad /**The effect of cholinergics on short-term memory and the excitability level of hippocampus circle structures.**/ Vliyaniye kholinergicheskikh veshchestv na kratkosrochnuyu pamyat' i uroven' vozbudimosti struktur gippokampova kruga. Farmakologiya i Toksikologiya (Moskva). 37(6):662-664, 1974.

The effect of pilocarpine and nicotine on short-term memory and the excitability of hippocampus circle structures was studied in dogs. Optimal doses of the cholinergics were found to improve short-term memory, lower the excitability level of the dorsal hippocampus and mamillary bodies, and to raise the excitability of the ventral hippocampus. 5 references. (Journal abstract modified)

208973 Migas, E. A.; Bul'on, V. V. Otdel farmakologii, laboratoriya eksperimental'noy farmakologii, Instituta eksperimental'noy meditsiny AMN SSSR, Leningrad **/The influence of ethymisol on the activity of adenylcyclase and 3', 5'-AMP-phosphodiesterase of rats' brains./** Vliyaniye etimozola na aktivnost' adeniltsiklazy i 3',5'-adenozinmonofosfatofosfodiesterazy mozga krys. Farmakologiya i Toksikologiya (Moskva). 37(6):710-711, 1974.

Adenylcyclase and 3', 5'-adenosine monophosphate (AMP) phosphodiesterase activity was investigated in rat brains after intramuscular injections of ethymisol. Ethymisol was found to elicit a repeated increase in adenylcylase activity 30 minutes after injections in doses of 25mg/kg. An increase in 3', 5'--AMP phosphodiesterase activity was concluded not to be dependent upon ethymisol influence on phosphodiesterase. 7 references.

208994 Palkovits, Miklos; Kobayashi, Ronald M.; Kizer, J. Steven; Jacobowitz, David M.; Kopin, Irwin J. Department of Anatomy, Semmelweis Medical University, 1450 Budapest, Tuzolto-u. 58., Hungary **Effect of stress on catecholamines and tyrosine hydroxylase activity of individual hypothalamic nuclei.** Bethesda, MD, National Institute of Mental Health, 1974. 15 p.

The effects of acute stress on norepinephrine (NE) and dopamine (DA) concentrations and effects of repeated stress on tyrosine hydroxylase (TH) activity were measured in individual hypothalamic nuclei and other rat brain regions. A microdissection technique and radioisotopic enzymatic assays were used. NE and DA concentrations were reduced and TH activity increased selectively in the arcuate nucleus. These results suggest that the arcuate nucleus may be selectively involved in the stress response and support the hypothesis that catecholamines in the medial basal hypothalamus mediate certain of the neuroendocrine changes observed in stress. 47 references. (Author abstract)

209032 Meshvelishvili, D. F. no address **/The influence of intraperitoneal injection of iprazide and transamine on the distribution of biogenic amines in cortical and subcortical white matter of the rat brain.** Vliyaniye intraperitoneal'nogo vvedeniya iprazida i transamina na raspredeleniye fonda biogennykh aminov v frontal'noy dole kory i belogo veshchestva podkorki mozga krys. Soobshcheniya Akademii Nauk Gruzinskoy SSR (Tbilisi). 76(2):453-455, 1974.

The influence of iprazide and transamine injected intraperitoneally on biogenic amine distribution in cortical and subcortical white matter was studied chromatographically in rat brains. Intraperitoneal injection of iprazide and transamine was found to cause psychoneural behavioral disturbances. An increase of serotonin and noradrenaline content in the cortical and subcortical white matter of the brain was observed. Comparatively small changes were noted in the quantitative distribution of adrenaline and dopamine. Improvement in psychoneural behavior was accompanied by an increase in content of biogenic amines. 7 references. (Journal abstract modified)

209351 Gupta, J. D.; Crollini, C. Children's Medical Research Foundation, Camperdown, N.S.W. 2050, Australia **Effect of lithium on magnesium-dependent enzymes.** Lancet (London). No.7900: 216-217, 1975.

The in vitro effect of lithium ions on the adenosine triphosphatase (ATPase) activity of chick blood and lens was studied. In lens mitochondrial fractions, only high concentrations of lithium depressed the sodium - potassium ATPase. The effect of lithium on sodium - potassium ATPase from red blood cells was less than from lens. No inhibition of magnesium ATPase was seen in either case. 9 references.

209352 Forrest, John N., Jr. Yale University School of Medicine, New Haven, CT **Lithium inhibition of cAMP-mediated hormones: a caution.** New England Journal of Medicine. 292(8):423-424, 1975.

A literature survey of lithium effects on various hormones is reported. Findings indicate that: 1) the hypothesis that lithium may be a general inhibitor of hormones mediated via the adenylate cyclase cyclic AMP system has not been substantiated; 2) lithium is not a universal inhibitor of hormones mediated by cyclic AMP; and 3) an inhibitory effect of lithium at a step beyond the formation of cyclic AMP is an established effect common to both thyroid stimulating hormone and vasopression. 14 references.

209728 Viala, D.; Valin, A; Buser, P. Laboratoire de Neurophysiologie, Universite de Paris VI, 9 quai St. Bernard, 75005 Paris **Relationship between the "late reflex discharge" and locomotor movements in acute spinal cats and rabbits with dopa.** Archives Italiennes de Biologie (Pisa). 112(4):299-306, 1974.

The effects of L-dopa on the late reflex discharge is studied in the rabbit. It is confirmed that, as previously shown in the cat, L-dopa causes depression of the short latency flexion reflex discharge elicited through stimulation of cutaneous afferents, and its replacement by a discharge of longer duration and longer latency. This observation is correlated with previous findings in rabbit showing that dopa can also elicit (in spinal preparations pretreated with a monoamines oxidase inhibitor) the development of organized sequences of rhythmic motoneurone activities mimikcing locomotion. After comparing the temporal evolution of the late discharge and that of locomotor like activities under the effect of dopa, it is concluded that both phenomena belong to the same category of neural events and may possibly have identical substrates. 8 references. (Author abstract modified)

209840 Collu, Robert; Letarte, Jacques; Leboeuf, Gilles; Ducharme, Jacques R. Div. of Endocrinology and Metabolism, Hopital Sainte-Justine, Montreal, Quebec, H3T 1C5, Canada **Endocrine effects of chronic administration of psychoactive drugs to prepuberal male rats. I: delta9-tetrahydrocannabinol.** Life Sciences. 16(4):533-542, 1975.

The endocrine effects of the chronic administration of delta9-tetrahydrocannabinol (delta9-THC) to prepuberal animals were studied by injecting intraperitoneally three times a week for a month either 1mg/kg or 10mg/kg of the psychoactive drug or the vehicle to groups of Sprague-Dawley male rats, starting at 21 days of age. After autopsy it was found that animals injected with 10mg/kg had smaller tails and prostates than controls. Plasma levels of growth hormone (GH) and luteinizing hormone (LH) were decreased in both groups while pituitary levels remained unmodified. Plasma levels of follicle stimulating hormone were not affected by the drug. The data

indicate that delta9-THC, the psychoactive ingredient of marihuana, when administered chronically to developing animals can inhibit the secretion of GH and LH and suppress prostate growth. 25 references. (Author abstract modified)

209961 Yehuda, Shlomo. Department of Psychology, Bar-Ilan University, Ramat-Gan, Israel **d-Amphetamine and the sensory role of a rat's tail in thermoregulation or what the rat's tail tells the rat's brain.** Behavioral Biology. 13(2):233-238, 1975.

Effects of the administration of d-amphetamine on the sensory role of a rat's tail in thermoregulation are examined. The importance of the tail's sensory role is demonstrated in tailless rats kept at various ambient temperatures, and in rats whose tail and body are exposed to different ambient temperatures. When the tail senses a cold ambient temperature (15-0 deg C), the body temperature increases, even if the rat itself is kept at room temperature (20 deg C). d-Amphetamine treatment enhances the hyperthermia induced by the tail's exposure to cold temperature and causes an impairment of the tail's thermal sensory role. 11 references. (Author abstract modified)

209962 Glick, Stanley D. Department of Pharmacology, Mount Sinai School of Medicine, City University of New York, New York, NY 10029 **Recovery of function and changes in sensitivity to amphetamine following caudate lesions in rats.** Behavioral Biology. 13(2):239-244, 1975.

In a study of the recovery of function and changes in sensitivity to amphetamine following caudate lesions, rats trained to bar press on a fixed interval 15 sec schedule for water reinforcement were administered various doses of d-amphetamine (0.25 - 4.0mg/kg) both before and 6-8 weeks after bilateral lesions of the caudate nucleus. Preoperatively, low doses of d-amphetamine increased responding and high doses depressed responding. Postoperatively, the d-amphetamine dose response curve was shifted to the left in rats with small caudate lesions and shifted to the right in rats with larger caudate lesions. Although both lesions produced initial impairments of bar pressing rates, only the larger lesion resulted in a persistent impairment. The lesion induced hypersensitivity and hyposensitivity to d-amphetamine were therefore associated with greater and lesser degrees of functional recovery, respectively. 6 references. (Author abstract modified)

210348 Erdosova, R.; Jakoubek, B.; Kraus, M. Czechoslovak Academy of Sciences, Institute of Physiology, Budejovicka, 14220 Prague 4 **Effect of stress and diazepam treatment during infancy on the corticosterone regulation and androgenic activity in adult male rats.** Experientia (Basel). 31(1):62-63, 1975.

The effect of stress and injection with diazepam during infancy on corticosterone regulation and androgenic activity was examined in adult male rats, and results indicated that stimulation of the adrenal cortex activity during the preweaning period can be followed by various changes in features of adult animals. Findings also demonstrate that adrenocorticotropic hormone (ACTH) treatment or stress stimulation during infancy that does not result in immediate gross damage to the young organism tends to favor such somatic aftereffects which are likely to be induced by higher androgenic activity, or conversely, the lack of extrastimulation or suppression of the response to undamaging stress by tranquilizers during the early stages of postnatal development is followed by indices of lower androgenic activity. 24 references.

210355 Meldrum, B. S.; Horton, R. W. Medical Research Council Neuropsychiatry Unit, Carshalton, Surrey, England **Cerebral functional effects of 2-deoxy-D-glucose and 3-O-methylglucose in rhesus monkeys.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 35(1):59-66, 1973.

The relationship between glucose availability and cerebral function was studied by assessing the effects of 2-deoxy-D-glucose and 3-O-methylglucose on behavior, the electroencephalograph (EEG) and cerebral arteriovenous differences. After intravenous infusion of 2-deoxy-D-glucose, a reduction in the apparent level of consciousness began after 1 to 3 minutes and was maximal after 3 to 15 minutes. EEG changes similar to those of moderate cerebral hypoxia and a fall in cerebral arteriovenous differences for oxygen, glucose and carbon dioxide occurred with the same time course. In some animals, EEG and clinical signs of epileptic activity appeared but with a longer latency. The behavioral and metabolic effects of 3-O-methylglucose (0.4-2.5g/kg) were similar to those of lower doses of 2-deoxy-D-glucose. The early EEG, behavioral and metabolic effects produced by both compounds are thought to result from competitive inhibition of glucose transport into the brain. Cerebral function thus appears to be as instantaneously dependent on glucose supply as on oxygen supply. 33 references. (Author abstract modified)

210599 Heiss, W.-D.; Hoyer, J. Institut fur allgemeine und vergleichende Physiologie, Schwarzspanierstrasse 17, A-1090, Wien, Austria **Dopamine receptor blockade by neuroleptic drugs in Aplysia neurones.** Experientia (Basel). 30(11):1318-1320, 1974.

The influence of haloperidol and mepazine on dopamine receptors was studied in ganglion preparations of the marine mollusc Aplysia californica by intracellular recording of neuronal activity and by extracellular microelectrophoretic application of the test substances. Results provide direct neurophysiological evidence for the blocking effect of the two antipsychotic drugs on dopamine receptors and agree with neurochemical, pharmacological and indirect physiological observations. 30 references.

210658 McGeer, P. L.; Grewaal, D. S.; McGeer, E. G. Department of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada **Influence of noncholinergic drugs on rat striatal acetylcholine levels.** Brain Research (Amsterdam). 80(2):211-217, 1974.

Rat striatal acetycholine levels were measured in rats following the administration of drugs that primarily affect dopamine metabolism. Reserpine, clozapine and chlorpromazine caused decreases in striatal acetycholine levels of 33%, 38% and 54% respectively. Apomorphine, l-dopa, methamphetamine and amantadine caused increases of 27%, 14%, 17% and 45% respectively. The decrease in acetycholine levels following drugs that deplete or block dopamine, and the increase following drugs that enhance dopamine or stimulate its receptors, is consistent with a direct inhibitory action of dopamine on cholinergic striatal interneurons. Increased levels of acetycholine would accompany decreased firing of cholinergic neurons due to dopaminergic inhibitory action. Decreased levels would accompany increased firing due to reduced dopaminergic inhibitory action. 33 references. (Author abstract)

210659 Gonzalez-Vegas, J. A. Escuela de Bioanalisis, Facultad de Medicina, Universidad Central de Venezuela, Caracas, Venezeula **Antagonism of dopamine-mediated inhibition in the nigro-striatal pathway: a mode of action of some catatonia-inducing drugs.** Brain Research (Amsterdam). 80(2):219-228, 1974.

Recordings were made from single neurons in the caudate nucleus of anesthetised rats. Dopamine (DA) was applied by iontophoresis to these neurons and its effects compared with those of substantia nigra (SN) stimulation. There was a good correlation between the inhibitory effects of SN stimulation and inhibitory actions of DA. Papaverine and bulbocapnine applied iontophoretically or given intravenously blocked the inhibitory effects of SN stimulation and of DA. The results provide evidence supporting the view that dopamine is the transmitter for the nigro-striatal pathway mediating inhibition in the rat. It is suggested that blockade of this pathway is one of the mechanisms by which bulbocapnine and papaverine produce catatonia. 34 references. (Author abstract)

210660 Kopin, Irwin J.; Palkovits, Miklos; Kobayashi, Ronald M.; Jacobowitz, David M. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Quantitative relationship of catecholamine content and histofluorescence in brain of rats.** Brain Research (Amsterdam). 80(2):229-235, 1974.

Levels of catecholamine content assayed by a sensitive radiometric technique were compared to semiquantitative visual estimation of the histofluorescence in different regions of rat brain after amine depletion by varying doses of reserpine. The range over which fluorescence of varicose terminals appeared to diminish is only about 20-40% of the normal catecholamine content. The level of this range varied with the area examined. The percent of normal catecholamine levels at which fluorescence was first noticed to be decreased from normal, and that at which flourescence seemed to disappear were relatively close and both appeared to be linearly correlated to the logarithm of the normal catecholamine content. In areas with a normally high catecholamine content, a greater percentage decrease in amine content was required to make a noticeable decrease in fluorescence than was required in areas with a normally lower catecholamine content. 12 references. (Author abstract)

210661 Palkovits, M.; Brownstein, M.; Saavedra, J. M. Department of Anatomy, Semmelweis Medical University, 1450 Budapest, Tuzolto-u 58, Hungary **Serotonin content of the brain stem nuclei in the rat.** Brain Research (Amsterdam). 80(2):237-249, 1974.

The serotonin (5-hydroxytryptamine; 5-HT) concentrations of 55 individual brainstem regions were determined by use of a specific and sensitive enzymatic isotopic technique in the rat. Serotonin was unevenly distributed throughout all the brainstem areas examined. The highest concentrations of 5-HT were found in certain of the raphe nuclei. A high amount of 5-HT was also measured in the substantia nigra and in the globus pallidus. The central and tegmental gray matters of the mesencephalon and pons contained moderate amounts of 5-HT. The nuclei of reticular formation all contained about the same amount of 5-HT. There was more than a fivefold difference between the highest and lowest concentrations of 5-HT measured in the cranial nerve nuclei. The motor nerve nuclei seemed to contain more of the amine than the sensory nerve nuclei. 17 references. (Author abstract)

210662 Baldwin, David M.; Haun, Charles K.; Sawyer, Charles H. Department of Anatomy, University of California Medical School, Los Angeles, CA 90024 **Effects of intraventricular infusions of ACTH1-24 and ACTH4-10 on LH release, ovulation and behavior in the rabbit.** Brain Research (Amsterdam). 80(2):291-301, 1974.

The effects of intraventricular (lateral and third ventricles) infusions of adrenocorticol stimula hormone (ACTH)1-24, ACTH4-10 and luteinizing hormone releasing hormone (LHRH) on behavior, LH release (by radioimmunoassay) and ovulation in the estrogen primed female rabbit. In addition, electroencephalographic (EEG) and multiple unit activity (MUA) recordings were made in various areas of the brain in six animals. In the first study, in which only limited behavioral observations were made due to the electrical recording procedures, ACTH1-24 was given 1 h after a control injection of saline, a sequence followed by ovulation. Under a similar infusion schedule (i.e.,saline infusion followed 2h later with ACTH1-24), a second group of animals were bled by cardiac puncture several times before and after saline and ACTH. None of these animals showed appreciable elevations in serum LH or ovulation, but two of five rabbits exhibited the stretching and yawning syndrome (SYS) and sexual behavior. In contrast, in trials involving animals given ACTH1-24 alone and subjected thereafter to multiple bleedings, five displayed sexual excitement, six demonstrated SYS, and six had elevations of serum LH with a peak 0.5-1.5h after infusion, of which five ovulated. Treatment with saline alone in nine rabbits had essentially no effect on these responses. 22 references. (Author abstract modified)

210664 Tauc, L.; Hinzen, D. H. Laboratoire de Neurobiologie Cellulaire, CNRS, 91190 Gif sue Yvette, France **Neuraminidase: its effect on synaptic transmission.** Brain Research (Amsterdam). 80(2):340-344, 1974.

A functional significance of sialic acid containing substances in synaptic transmission is described. Neuraminidase was injected into a presynaptic neuron of the buccal ganglion of Aplysia californica and synaptic activity was monitored in the postsynaptic cell. It is suggested that neuraminidase may effect the mechanisms of transmitter synthesis and storage. The amplitudes of the synaptic potentials started to decrease about 2-4 hours after the intracellular application of the enzyme. The results indicated that the influx of calcium ions into the presynaptic terminal could be controlled by the sialic acid containing substances and thus be inhibited by the action of neuraminidase. It is concluded that the neuraminidase acts at the presynatic terminal specifically by preventing release of transmitter. 21 references.

210665 Fjerdingstad, E. J.; Danscher, Gorm; Fjerdingstad, Erik. Institute of Anatomy, University of Aarhus, Aarhus, Denmark **Hippocampus: selective concentrations of lead in the normal rat brain.** Brain Research (Amsterdam). 80(2):350-354, 1974.

The selective concentrations of lead in the normal rat brain is described. Timm staining in the hippocampal mossy fiber system was found to be due to high levels of lead. The concentrations of lead in the hippocampus was 10 times higher than that of the rest of the brain. It was concluded that the high hippocampal levels did not seem to be due to high lead exposure or high lead in the food. 14 references.

210668 Ladinsky, H.; Consolo, S.; Bianchi, S.; Samanin, R.; Ghezzi, D. Istituto di Ricerche Famacologiche 'Mario Negri', 20157 Milan, Italy **Cholinergic-dopaminergic interaction in the striatum: the effect of 6-hyrdroxydopamine or pimozide treatment on the increased striatal acetylcholine levels induced by apomorphine, piribedil and d-amphetamine.** Brain Research (Amsterdam). 84(2):221-226, 1975.

The effect of 6-hydroxydopamine or pimozide treatment on the increased striatal acetylcholine levels induced by apomorphine, piribedil and d-amphetamine were examined. Apomorphine and d-amphetamine increased rat striatal acetylcholine

levels without affecting choline. Pretreatment with pimozide completely antagonized the effect of apomorphine and piribedil and by itself markedly decreased striatal acetylcholine levels. D-Amphetamine significantly antagoniseD the effect of pimozide. Nine days after pretreatment with 6-hydroxydopamine plus pargyline, striatal dopamine was decreased by 78% while acetylcholine and choline levels remained unaltered. Under these conditions, the effect of d-amphetamine was completely abolished while apomorphine and piribedil were just as active as in the vehicle treated group. The results suggest that d-amphetamine acted indirectly to increase striatal acetylcholine levels probably through the release of dopamine and/or noradrenaline, while apomorphine and piribedil acted directly at dopamine receptor sites. 29 references. (Author abstract)

210669 Guyenet, P. G.; Agid, Y.; Javoy, F.; Beaujouan, J. C.; Rossier, J.; Glowinski, J. Laboratoire de Biologie Moleculaire, College de France, 11, Place Marcelin Berthelot, 75231 Paris Cedex 05, France **Effects of dopaminergic receptor agonists and antagonists on the activity of the neo-striatal cholinergic system.** Brain Research (Amsterdam). 84(2):227-244, 1975.

The effects of various neuroleptics and of apomorphine on the metabolism of acetylcholine (ACh) were examined in the neostriatum of the rat. A specific radioenzymatic assay for brain ACh was used. The rat neostriatal ACh levels were decreased by neuroleptics of the phenothiazine and butyrophenone type and increased by apomorphine. An in vivo estimation of the rate of utilization of ACh was obtained by measuring the decline in neostriatal ACh content following the local microinjection of hemicholinium-3. This compound blocked almost totally the synthesis of ACh in these conditions. Chlorpromazine enhanced neostriatal ACh utilization and apomorphine antagonized this effect. Neuroleptics did not affect ACh levels in the parietal cerebral cortex and the hippocampal formation. The results suggest that dopaminergic receptors as defined by their pharmacological interaction with neuroleptics and apomorphine are localized on neostriatal ACh neurons. 61 references. (Author abstract modified)

210670 Black, Ira B.; Reis, Donald J. Laboratory of Neurobiology, Department of Neurology, Cornell University Medical College, 1300 York Ave., New York, NY 10021 **Ontogeny of the induction of tyrosine hydroxylase by reserpine in the superior cervical ganglion, nucleus locus coeruleus and adrenal gland.** Brain Research (Amsterdam). 84(2):269-278, 1974.

The ontogeny of the induction of tyrosine hydroxylase by reserpine has been studied in the superior cervical ganglion, adrenal gland and nucleus locus coeruleus of the rat. The inductive response developed gradually over a period of days in all three areas. However, the onset of induction occurred at markedly different times in these regions, being present from day 2 of life, the earliest time tested, in the adrenal day six in the locus coeruleus and day 24 in the ganglion. In the ganglion even extremely high, toxic doses of reserpine failed to induce the enzyme during the first 3 weeks of life. Decentralization studies indicated that the ganglion was functionally innervated at this time. Moreover, the onset of induction was not time locked to a specific phase of the postnatal development of tyrosine hydroxylase activity in the areas examined. It is probable that the development of inducibility reflects maturation of mechanisms intrinsic to the adrenergic cell, and this timetable is different for cells in different areas. 25 references. (Author abstract)

210672 Myers, R. D.; Waller, M. B. Laboratory of Neuropsychology, Purdue University, Lafayette, IN 47907 **5-HT- and norepinephrine induced release of ACh from the thalamus and mesencephalon of the monkey during thermoregulation.** Brain Research (Amsterdam). 84(1):47-61, 1975

In the unanesthetized pigtailed monkey (Macaca nemestrina), trained to sit in a primate chair, the body temperature was monitored from the brain and colon. The perfusate was an artical cerebrosponal fluid containing the anticholinesterase neostigmine; each sample of effluent was assayed for the content of acetylcholine (ACh) on the eserinized guinea pig ileum. The microinjectioon of 5-HT and norepinephrine into the monkey's hypothalamus evoked a rise or fall in body temperature. These amines caused a concurrent change in the release of ACh at perfusion loci in both thalamus and mesencephalon. A composite anatomical mapping of the active releasing sites revealed that the output of ACh was elevated at 19 of 36 sites during the 5-HT induced hyperthermia. The region of maximum sensitivity to 5-HT in terms of the percent change in ACh output at thalamic and mesencephalic sites was the rostral hypothalamus. These results provide further support for a neurochemical model of thermoregulation which postulates that 5-HT activates a cholinergic pathway originating in the hypothalamus which transmits the efferent signals for heat production. 29 references. (Author abstract modified)

210673 Morgan, William W.; Saldana, John J.; Yndo, Catherine A.; Morgan, Joy F. Department of Anatomy, University of Texas Health Science Center, San Antonio, TX 78284 **Correlations between circadian changes in serum amino acids or brain tryptophan and the contents of serotonin and 5-hydroxyindoleacetic acid in regions of the rat brain.** Brain Research (Amsterdam). 84(1):75-86, 1975.

Circadian changes in tryptophan, serotonin (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) were investigated in the cerebral cortex and the brain stem of male rats previously exposed to a 14:10light - dark (LD) lighting regimen. Statistically significant circadian changes in 5-HIAA were observed in the cerebral cortex of the control and the experimental animals and in the brain stem of the experimental animals. Circadian changes in tryptophan were observed in the cortex and brain stem of control animals, but the magnitude of the daily changes in tryptophan in experimental animals was comparatively reduced so that a statistically significant change was observed only in the brain stem. Highly statistically significant correlations were demonstrated between brain tryptophan and 5-HIAA suggesting a possible interrelationship between these parameters. Circadian changes in 5-HT were observed in the cerebral cortex of the experimental and in the brain stem of control animals. The inconsistency of the 5-HT rhythms may be a reflection of the daily disturbance of the animals. Significant circadian changes in free and also total plasma tryptophan were observed in both the control and experimental animals. 24 references. (Author abstract modified)

210675 Leibowitz, Sarah Fryer. Rockefeller University, New York, NY 10021 **Amphetamine: possible site and mode of action for producing anorexia in the rat.** Brain Research (Amsterdam). 84(1):160-167, 1975.

The site and mode of action of amphetamine (AMPH) in producing anorexia in the rat was investigated by injecting AMPH directly into the brain through permanently implanted cannulas. The effects on feeding behavior of AMPH administered into 20 different areas throughout the mesencephalon, diencephalon and telencephalon were examined. The results indicated that centrally injected AMPH is effective in

producing anorexia, with the effect primary localized at one particular brain area, the lateral portion of the hypothalamus. The anorexia induced by lateral hypothalamus injection of AMPH was abolished by locally administered beta-adrenergic and dopaminergic receptor blockers. 31 references.

210696 Thomsen, Klaus. Psychopharmacology Research Unit, Aarhus University Psychiatric Institute, DK-8240 Risskov, Denmark **The effect of sodium chloride on kidney function in rats with lithium intoxication.** Acta Pharmacologica et Toxicologica (Kobenhavn). 33(2):92-102, 1973.

The effect of lithium was studied in three groups of rats given food containing 20, 40, or 60mmol LiCl/kg dry weight for 3-4 weeks. The rats with low and medium lithium intakes could be maintained at this level for a very long time. In the rats with a high lithium intake the serum lithium concentration after 2-3 weeks rose to high values as a result of a decrease in the renal lithium clearance; the rats developed severe lithium intoxication. The results indicate that the decrease in lithium clearance produced by prolonged administration of high lithium doses is not due to irreversible kidney damage; it can be reversed by the administration of sodium. The development of severe intoxication can also be prevented by administering sodium along with lithium. These observations support the hypothesis that sodium depletion plays an important role in the development of severe lithium intoxication. 10 references. (Author abstract modified)

210699 Agid, Yves; Javoy, France; Glowinski, Jacques. Groupe NB (INSERM U. 114), College de France, Paris 5 **Chemical or electrolytic lesion of the substantia nigra: early effects on neostriatal dopamine metabolism.** Brain Research (Amsterdam). 74(1):41-49, 1974.

Dopamine metabolism was investigated in rats subjected to a unilateral 6-hydroxydopamine injection or to an electrolytic lesion in the right substantia nigra. Nigral chemical or electrolytic lesions induced the following changes in the ipsilateral neostriatum, when compared to the contralateral neostriatum. An immediate increase in the dopamine content and in the initial accumulation of (3H)-dopamine newly synthesized from L-(3,5-3H)tyrosine injected intravenously and a prevention of the initial decrease in dopamine content induced by inhibition of dihydroxyphenylalanine (DOPA) decarboxylase (Ro4-4602) were observed. An activation of tyrosine hydroxylation as indicated by the increased initial accumulation of (3H)H2O formed in vivo from locally injected L-(3,5-3H)tyrosine was found. An increased dopamine content and synthesis were also detected after the systemic injection of gamma-hydroxybutyrate, an anesthetic known to interrupt nerve activity in the nigro - neostriatal dopaminergic system. It is concluded that the changes in dopamine levels observed shortly after chemical or electrolytic lesion of the substantia nigra as well as after the peripheral injection of gamma-hydroxybutyrate result from both a decreased utilization and a stimulated synthesis of dopamine. 24 references. (Author abstract modified)

210700 Kerr, Frederick W. L.; Triplett, Joseph N., Jr.; Beeler, George W. Section of Neurologic Surgery, Mayo Clinic, Rochester, MN 55901 **Reciprocal (push-pull) effects of morphine on single units in the ventromedian and lateral hypothalamus and influences on other nuclei: with comment on methadone effects during withdrawal from morphine.** Brain Research (Amsterdam). 74(1):81-103, 1974.

The effects of morphine and of its antagonists naloxone and nalorphine on multiple single units recorded simultaneously in the ventromedian nucleus (VMN) and in the lateral hypothalamic area (LHA) and certain other neuronal groups were investigated in naive and morphine dependent adult rats using pulse height analysis techniques and computer generated firing frequency histograms. Morphine produced diametrically opposite effects on VMN and LHA in both naive and dependent animals; with the exception of a few units, neurons recorded from the VMN were excited by morphine and, conversely, those in LHA were inhibited; the antagonists naloxone and nalorphine produced clear cut reversal of these effects. During withdrawal phases in addicted animals, firing rates in the LHA were greater than rates recorded in the same area of naive animals; no significant differences between firing rates in the VMN of naive and addicted animals were observed. Methadone effects were investigated in morphine dependent rats in withdrawal; both VMN and LHA neurons were excited by methadone and the effect of morphine on these nuclei was reversed. 34 references. (Author abstract modified)

210701 Dolezalova, Hana; Stepita-Klauco, Matej. Lab. of Neuropsychopharmacology Department of Biobehavioral Sciences, University of Connecticut, Storrs, CT 06268 **Piperidine concentration changes in the brain and blood of dormant mice.** Brain Research (Amsterdam). 74(1):182-184, 1974.

Concentration changes of piperidine which occur during dormancy (apparent sleep) in major parts of the mouse brain and in blood were examined. During a 30 min dormancy, the piperidine concentration in the blood and in all assayed parts of the brain increased by more than 10 times. The increase of piperidine in whole mouse brain during dormancy in the blood of dormant mice was large enough to account for the increase in the concentration in the prosencephalon and in the cerebellum. In the mesencephalon the tissue concentration was three times that found in the blood of dormant mice. An active transport of piperidine, and piperidine synthesis within the mesenecephalon is suggested to explain the results. 6 references.

210703 Sasa, Masashi; Munekiyo, Katsunori; Ikeda, Hitoshi; Takaori, Shuji. Department of Pharmacology, Faculty of Medicine, Kyoto University, Sakyo-ku, Kyoto 606, Japan **Noradrenaline-mediated inhibition by locus coeruleus of spinal trigeminal neurons.** Brain Research (Amsterdam). 80(3):443-460, 1974.

Inhibitory effects of conditioning stimulation of the locus coeruleus (LC) on the neuron activity in spinal trigeminal nucleus (STN) were investigated in gallamine immobilized cats. Conditioning stimuli were applied to LC and sensory cortex (SC) at various conditioning stimuli - test stimulus (C-T) intervals. In tracking experiments near the LC region, conditioning stimulation of LC itself produced the most pronounced decrease in amplitude of the STN field potentials. Orthodromic spikes of STN single neurons were significantly reduced by conditioning stimulation of LC as well as SC. In reserpine treated animals, however, conditioning stimulation of LC failed to produce a decrease in the number of orthodromic spikes, while the inhibitory effect of SC conditioning stimulation remained unaffected. Under these circumstances, intravenous L-dopa and intraventricular noradrenaline reproduced an inhibitory effect of LC conditioning stimulation on orthodromic spike generation, while such an effect was not seen with either dopamine or serotonin. Antidromic spike was unaltered by any of these treatments. These results strongly suggest that noradrenaline released from the terminals of neurons originating in LC produces an inhibition of transmission in the STN relay neurons. 32 references. (Author abstract modified)

210710 Mosko, Sarah; Jacobs, Barry L. Department of Psychology, Princeton University, Princeton, NJ 08540 **Effect of peripherally administered serotonin on the neuronal activity of midbrain raphe neurons.** Brain Research (Amsterdam). 79(2):315-320, 1974.

The effect of peripherally applied 5-hydroxytryptamine (5-HT) on unit activity in the dorsal and median raphe nuclei was studied in 32 adult rats. Raphe cells responded almost uniformly to i.p. 5-HT by an increase in firing rate which became evident within 10 minutes of injection. The raphe units responsed in a dose dependent fashion. The failure of peripherally administered 5-HT to depress the raphe neuron activity indicates that it does not mimic the central action of 5-HT on serotonin containing neurons. Lysergic acid diethylamide injection produced a reversible depression of unit activity within 30 sec. 32 references.

210713 Sorimachi, Masau; Miyamoto, Kanji; Kataoka, Kiyoshi. Department of Physiology, Ehime University School of Medicine, 790 Matsuyama, Japan **Postnatal development of choline uptake by cholinergic terminals in rat brain.** Brain Research (Amsterdam). 79(2):343-346, 1974.

The mode of choline transport in developing rat brains was examined. At earlier stages a low concentration of choline was selectively accumulated by cholinergic terminals. In the hippocampus, the increase of choline uptake activity preceded that of choline acetyltransferase activity by about 4 days. It is suggested that the delay of the choline acetyltransferase increase in the hippocampus reflects the time required for axoplasmic transport of newly synthesized enzyme to the nerve terminals. It is concluded that choline uptake activity during development is an earlier index of cholinergic synaptogenesis than the choline acetyltransferase activity, although the latter is more intimately related to the functional maturation of cholinergic transmission. 17 references.

210740 Viala, D.; Buser, P. Laboratoire de Neurophysiologie Comparee, Universite de Paris VI, 4, Place Jussieu, f-75230 Paris Cedex 05, France **Effects of a decarboxylase inhibiter on the Dopa and 5-HTP induced changes in the locomotor-like discharge pattern of rabbit hind limb nerves.** Psychopharmacologia (Berlin). 40(3):225-233, 1974.

The hypothesis that the effects of decarboxylase inhibitor on the Dopa and 5-hydroxytryptophan (5-HTP) induced changes in the locomotor like discharge of rabbit hindlimb nerves was examined. Animals were given Ro4-4602, an inhibitor of Dopa and 5-HTP decarboxylase (DC) at low and high doses. Low doses had a potentiating action on the 5-HTP and Dopa effects, while high doses delayed their action. Assuming that at low dosage the inhibitor was acting on the peripheral DC and at high doses on both the peripheral and central DC, it may be concluded that the precursors act centrally through transformation into serotonin (5-HT) and dopamine or noradrenaline respectively. 13 references. (Author abstract modified)

210744 Moniuszko-Jakoniuk, Janina; Wisniewski, Konstanty. Department of Pharmacology, Medical School, PL-15-222 Bialystok, Poland **The activation of the kinin forming system and the effects of thiopental.** Psychopharmacologia (Berlin). 40(3):269-277, 1974.

The effects of activation of kinin forming enzymes on the potency of thiopental were studied. The psychodepressive action of thiopental was increased in animals to which bradykinin had been given or in which the kinin forming enzymes of the central nervous system had been activated with kallikrein. From these results the altered potency of thiopental does not seem to depend on its higher level in the effector organ or on a changed binding ability with the brain tissue proteins, but the potentiation may originate from an altered metabolism or changed neurohormonal background of the brain tissue due to the effects of bradykinin or kallikrein. 18 references. (Author abstract)

210747 Huang, Jen-Tzaw; Ho, Beng T. Department of Pharmacology, University of Minnesota, Minneapolis, MN 55455 **Some pharmacological actions of 2,5-dimethoxy-4-ethylamphetamine (DOET) in rats and mice.** Journal of Pharmacy and Pharmacology (London). 27(1):18-22, 1975.

In a study of the pharmacological actions of 2,4-dimethoxy-4-ethylamphetamine (DOET), the drug exhibited pressor action in rats. This increase of blood pressure was blocked by pretreatment with cinanserin. DOET at high doses decreased the spontaneous locomotor activity of mice at the first hour but increased the activity at the second hour; a low dose was less effective. DOET also increased the rectal temperature of rats and this hyperthermic action was suppressed by pretreating the animals with cinanserin or methysergide. These actions of DOET were compared with those of 2,5-dimethoxy-4-methylamphetamine (DOM). 13 references. (Author abstract)

210749 Freeman, J. J.; Sulser, F. Department of Pharmacology, UCLA School of Medicine, Los Angeles, CA 90024 **The role of p-hydroxylation of amphetamine in its peripheral mode of action.** Journal of Pharmacy and Pharmacology (London). 27(1):38-42, 1975.

The hypothesis that the hydroxylated metabolites of amphetamine, p-hydroxyamphetamine and p-hydroxynorephedrine, major metabolites in some species, may mediate the peripheral cardiovascular effects of the parent drug was tested. Desipramine completely abolished the blood pressure response to (+)-amphetamine in the rat, whereas the tricyclic antidepressant iprindole did not reduce this response. Since both tricyclic drugs inhibit the aromatic hydroxylation of amphetamine, the hypothesis that hydroxylated metabolites of amphetamine, p-hydroxyamphetamine and p-hydroxynorephedrine are essential for the peripheral sympathomimetic effects of amphetamine was not supported. 22 references. (Author abstract modified)

210751 Smith, Alfred A.; Engelsher, Charles; Crofford, Marsha. Departments of Psychiatry and Pharmacology, New York Medical College, New York, NY 10029 **Modulation of the respiratory depressant effect of ethanol by 5-hydroxytryptamine.** Journal of Pharmacy and Pharmacology (London). 27(1):60-61, 1975.

The mechanisms of respiratory depression induced in the mouse by alcohols, two barbiturates and an opioid using blood gas analysis were examined. Results suggest that certain alcohols, notably ethanol, require 5-hydroxytryptamine (5-HT) to induce respiratory depression in the mouse. The reductive catabolite of 5-HT appears to play little or no role since the injection intracerebrally of 5-hydroxytryptophol failed to restore the ability of ethanol to produce respiratory depression in mice pretreated with reserpine. The finding that 5-HT mediates or modulates respiratory depression induced by a series of alcohols but not by two barbiturates or methadone suggests alcohols differ from two other kinds of narcotics at least in regard to respiratory depression. The failure of paraldehyde or chloral hydrate to share a common neurotransmitter mechanism with ethanol is surprising. 1 reference.

210753 Da Prada, M.; Obrist, R.; Pletscher, A. Research Department, F. Hoffman-La Roche & Co. Ltd., Basel, Switzerland **Accumulation of acetylcholine and aromatic monoamines by interaction with adenosine-5'-triphosphate.** Journal of Pharmacy and Pharmacology (London). 27(1):63-66, 1975.

The accumulation of acetylcholine and aromatic amines by the interaction with adenosine-5'-monophosphate (AMP) was examined. The findings confirm that amines can accummulate by mere physiochemical interaction against an apparent concentration gradient in a compartment containing ATP, provided it is surrounded by a membrane impermeable to this nucleotide, but permeable to the amines. Results showed that a concentration gradient was built up not only with aromatic monoamines but also with acetylcholine and its precursor choline. This indicates that acetylcholine and choline both interact with ATP. The maximum concentration gradients observed varied for the different amines; for instance, geh gradient was higher with histamine, tryptamine and tyramine than with noradrenaline, dopamine and 5-hydroxytryptamine. It is concluded that the acummulation of biogenic amines, including acetylcholine, in subcellular storage organelles is probably due not only to an active transport at the granular membrane level but also to a binding of the amines to intragranular ATP. 12 references.

210759 Versteeg, Dirk H. G.; van Ree, Jan M.; Provoost, Abraham P.; deJong, Wybren. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Utrecht, The Netherlands. **Neonatal 6-hydroxydopamine treatment: noradrenaline levels and in vitro 3H-catecholamine synthesis in discrete brain regions of adult rats.** Life Sciences (Oxford). 15(12):2127-2134, 1974.

The effect of neonatal 6-hydroxydopamine on noradrenaline levels and in vitro catecholamine synthesis in discrete brain regions of adult rats was examined. Endogenous noradrenaline levels are elevated in medulla oblongata, mesencephalon, pons and thalamus of adult rats which had been treated with 6-hydroxydopamine on days 1, 2, 8 and 15 after birth. Levels in spinal cord, cerebellum, hippocampus/amygdala and cortex are depressed, whereas no significant changes are observed in striatum, hypothalamus and medulla spinalis. The rate at which medulla oblongata synthesizes tritiated noradrenaline and dopamine from tritiated tyrosine in vitro is markedly enhanced. No effect was apparent on catecholamine synthesis in hypothalamus. Tritiated noradrenaline synthesis, but not tritiated dopamine synthesis, in the cortex is depressed. These results support the view that neonatal 6-hydroxydopamine treatment causes a degeneration of noradrenaline nerve terminals in the cortex and induces an increase in noradrenaline terminals in the medulla oblongata. 17 references. (Author abstract)

210760 Paul, Steven M.; Hsu, Louise L.; Mandell, Arnold J. Department of Psychiatry, University of California, San Diego, La Jolla, CA 92037 **Extrapineal N-acetyltransferase activity in rat brain.** Life Sciences (Oxford). 15(12):2135-2143, 1974.

An extrapineal enzyme that N-acetylates a variety of indole and catechol alkylamines, including the psychoactive drugs mescaline and d-amphetamine, was partially purified from rat brain. This enzymatic activity has a distinct pH optimum, is linear with incubation time and protein concentration, and is abolished by heating. Purification is approximately ten fold with ammonium sulfate precipitation and column chromatography, yielding a specific activity of 7936 pmoles of product per mg of protein per hour with tryptamine as substrate. 31 references. (Author abstract)

210761 Doggett, N. S.; Reno, H.; Spencer, P. S. J. Department of Applied Pharmacology, Welsh School of Pharmacy, UWIST, Cardiff, Wales **Possible involvement of 5-hydroxytryptamine in the antidepressant activity of narcotic analgesics.** Neuropharmacology (Oxford). 14(2):81-84, 1975.

The interaction of some clinically established antidepressants with 5-hydroxytryptamine (5-HT) within the brain was studied and their properties were compared with those of morphine, cyclazocine and naloxone. The intraperitoneal injection of 5-hydroxytryptophan (5-HTP) elicits in mice a head twitching reaction which is proportional to the amount of free 5-HT within the brain. This effect is markedly potentiated by the monoamine oxidase inhibitor isocarboxazid and attenuated by (+)-amphetamine and desmethylimipramine. The narcotic agonist morphine, the partial agonist cyclazocine and the antagonist naloxone were examined for their effects upon this head twitching reaction and each of these three agents antagonized it. Although the drugs studied do not have identical effects upon the central excitatory effects of 5-HT, an interaction with this amine is common to all and, in view of the various hypotheses linking clinical depression with abnormal indole metabolism, it may be of importance in any antidepressant activity possessed by them. 10 references. (Author abstract modified)

210764 Green, A. R.; Grahame-Smith, D. G. MRC Unit, Radcliffe Infirmary, Oxford OX2 6HE, England **The effect of diphenylhydantoin on brain 5-hydroxytryptamine metabolism and function.** Neuropharmacology (Oxford). 14(2)107-113, 1975.

In a study of 5-hydrodytraptamine (5-HT) metabolum, it was found that diphenylhydantoin (DPH) enhanced the hyperactivity syndrome produced by monoamine oxidase inhibition and tryptophan administration to the rat. One dose of DPH alone had no effect on 5-HT synthesis and did not enhance the hyperactivity resulting from administration of the suggested 5-HT agonist 5-methoxy-N,N-dimethyltryptamine. This argues against DPH altering acutely the postsynaptic responses to released 5-HT. Administration of DPH twice daily for 2 days increased the rate of 5-HT synthesis by 100%. Chlorimipramine, which inhibits 5-HT reuptake, also enhanced the hyperactivity but decreased 5-HT synthesis by 50% when given on the same regimen. This suggests that DPH is not altering 5-HT reuptake. Antiepileptic drugs structurally similar to DPH did not potentiate the hyperactivity syndrome. It is suggested that DPH alters the amount of 5-HT that is released and is active at the nerve ending. The apparent similarities in action between lithium and DPH on 5-HT function and metabolism are noted and a possible common mechanism of action suggested. 20 references. (Author abstract modified)

210765 Gerald, M. C.; Hsu, S. Y. Division of Pharmacology, College of Pharmacy, Ohio State University, Columbus, OH 43210 **The effects of amphetamine isomers on neuromuscular transmission.** Neuropharmacology (Oxford). 14(2):115-123, 1975.

The effects of (+)- and (-)-amphetamine on neuromuscular transmission were evaluated by monitoring twitch tension elicited by direct and/or indirect stimulation of the isolated rat phrenic nerve - diaphragm preparation. Low concentrations of these isomers facilitated twitch, while higher concentrations caused dose dependent blockade in nerve stimulated preparations. Tachyphylaxis developed to the facilitatory effects of (+)-amphetamine on twitch tension; a progressive enhancement in the rate and magnitude of depression was observed with successive doses. (+)-Tubocurarine or succinylcholine in combination with amphetamine produced mutually enhanced

blockade of twitch. These results suggest that amphetamine induced muscle weakness in high doses and enhancement in physical endurance and in performance in moderate doses may result, at least in part, from a peripheral component. Amphetamine's actions on neuromuscular transmission are complex and may be the consequence of interactions with adrenergic and/or cholinergic systems. 17 references. (Author abstract modified)

210766 Koslow, S. H.; Bjegovic, M.; Costa E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Catecholamines in sympathetic ganglia of rat: effects of dexamethasone and reserpine.** Journal of Neurochemistry (Oxford). 24(2):277-281, 1975.

The effects of dexamethasone and reserpine on the sympathetic ganglia of the rat were examined. The superior cervical sympathetic ganglion of rats contains a finite amount of epinephrine all of which is of ganglionic origin. Treatment of newborn rats with dexamethasone for 8 days results in a 112 fold increase in the epinephrine concentration, whereas the norepinephrine and dopamine are increased by only 1.4and 1.9fold respectively. This epinephrine increase in newborn rats is reversible if treatment is discontinued, and it fails to occur in adult animals. The epinephrine store of normal and dexamethasone treated animals is resistant to the depletion by reserpine. There is no increase in the epinephrine content in organs innervated by axons emanating from the ganglion. The data presented support the localization of epinephreine in small intensely fluorescent cells in the ganglion; it is proposed that epinephrine may be released from these cells and function as a modulator of ganglionic transmission. 18 references. (Author abstract)

210769 Sarkar, C.; Ghosh, J. J. Department of Biochemistry, University of Calcutta, Calcutta 19, India **Effect of delta9-tetrahydrocannabinol administration on the lipid constituents of rat brain subcellular fractions.** Journal of Neurochemistry (Oxford). 24(2):381-385, 1975.

The effects of acute and chronic treatment with delta9-tetrahydrocannabinol (THC) administration by the intraperitoneal route on the cholesterol, cerebroside and individual phospholipid contents in microsomal, synaptosomal, mitochodrial and myelin fractions from adult rat brain is reported. The drug has been found to affect the different subcellular membranous lipid and phospholipid components in a characteristic manner. 34 references. (Author abstract)

210770 Lamble, Andrea P.; Lamble, J. W. Smith & Nephew Research, Ltd., Gilston Park, Harlow, Essex, England **Some effects of pilocarpine and acetylcholine on the responses of the guinea-pig vas deferens to hypogastric nerve stimulation and transmural stimulation and applied (-)-noradrenaline.** Journal of Pharmacy and Pharmacology (London). 27(2):79-87, 1975.

Enhancement by acetylcholine and by pilocarpine of the contractile responses of the guinea pig isolated vas deferens to hypogastric nerve and transmural stimulation and to exogenous (-)-noradrenaline was examined. At high concentration, acetylcholine enhanced responses in hypogastric nerve, transmural, and exogenous (-)-noradrenaline, in descending order of effect. Pilocarpine produced a similar maximal degree of enhancement with all three stimuli. All these effects were reversibly inhibited by atropine, at a concentration which alone did not affect responses to the stimuli. Pilocarpine gave a concentration - related inhibition of the enhancement of responses to hypogastric nerve stimulation by 600nM acetylcholine. 29 references. (Author abstract)

210771 Blumberg, J. B.; Taylor, R. E.; Sulser, F. Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37217 **Blockade by pimozide of a noradrenaline sensitive adenylate cyclase in the limbic forebrain: possible role of limbic noradrenergic mechanisms in the mode of action of antipsychotics.** Journal of Pharmacy and Pharmacology (London). 27(2):125-128, 1975.

The concentration of noradrenaline which produces a marked increase in the level of cyclic adenosine monophosphate (AMP) is reported. The results demonstrate the occurrence in slices of the limbic forebrain of a noradrenaline but not dopamine or 5-hydroxytryptamine sensitive adenylate cyclase and show that the noradrenaline induced increase in cyclic AMP in this area of the brain is blocked by low concentrations of pimozide. It is concluded that pimozide is not a selective dopamine blocking agent. 28 references.

210772 Broekkamp, C. L. E.; Weemaes, Andrea J. M.; van Rossum, J. M. Department of Pharmacology, University of Nijmegen, Geert Grootplein Noord 21, Nijemegen, The Netherlands **Does fenfluramine act via norfenfluramine?** Journal of Pharmacy and Pharmacology (London). 27(2):129-130, 1975.

The possible central action of fenfluramine and its metabolite norfenfluramine was examined by injecting of small amounts directly into the brain of rats. Even high dosages of fenfluramine are inactive when administered via the intracerebral route. Under identical conditions norfenfluramine is active in moderate doses. There was a significant difference in the amounts of rice eaten by the rats with nucleus interstitialis cannulae and those with neostriatal cannulae after norfenfluramine administration. The findings add substance to the suggestion that the central anorectic properties of fenfluramine are mediated mainly by norfenfluramine. 12 references.

210776 Di Chiara, G.; Balakleevsky, A.; Porceddu, M. L.; Tagliamonte, A.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Cagliari, Italy **Inhibition by apomorphine of dopamine deamination in the rat brain.** Journal of Neurochemistry (Oxford). 23(6):1105-1108, 1974.

The inhibition by apomorphine of the dopamine deamination was examined in the rat brain. Apomorphine (A) inhibited dopamine deamination by rat brain mitochondria, but did not influence catechol-O-methyltransferase (COMT) activity by brain homogenates. The administration of apormorphine to normal rats increased brain dopamine (DA) by 34% and decreased homovanillic acid (HVA) and dihydroxyphenylacetic acid (DOPAC) by 60%. In rats treated with reserpine 15 min prior to A, the latter prevented the rise of cerebral HVA and DOPAC and the depletion of DA produced by the former. A decreased the L-DOPA induced accumulation of HVA and DOPAC in the rat basal ganglia. These results indicate that A inhibits DA deamination by monoamine oxidase. 32 references. (Author abstract modified)

210779 Krivanek, J. Institute of Physiology, Czechoslovak Academy of Sciences, Prague **Changes in the neuronal protein labelling induced by potassium ions in vivo (spreading depression).** Journal of Neurochemistry (Oxford). 23(6):1255-1262, 1974.

Inhibition of incorporation of labelled leucine into the protein of the cerebral cortex induced by potassium ions in vivo (spreading depression) was analyzed in isolated neuronal perikarya and compared with that in the whole cortex. Parti-

tion of proteins and amino acids and their radioactivities between tissue (cells) and incubation and disintegration media were checked at various steps of the separation procedure. The effect of potassium ions elicited in vivo persisted through all the steps of separation through to the neuronal perikarya pellets. The inhibition of amino acid incorporation was found to be less pronounced in perikarya than in the whole cortex. The validity of the separation method for the study of metabolic changes induced in vivo and possible participation of the glial cells in cerebral cortical responses to enhanced extracellular potassium are discussed. 38 references. (Author abstract)

210780 Mohler, H.; Patel, A. J.; Balazs, R. F. Hoffman-La Roche A. G., Research Department, Basel, Switzerland **Metabolic compartmentation in the brain: metabolism of a tricarboxylic acid cycle intermediate, (1,4-14C)succinate, after intracerebral administration.** Journal of Neurochemistry (Oxford). 23(6):1281-1289, 1974.

The metabolism of a tricarboxylic acid cycle (cycle) intermediate (1,4-14C)succinate, was studied in the brain at 2-20 min after intracerebral injection. The oxidation of (14C)succinate was rapid, as shown by the incorporation of 14C into cycle amino acids which accounted for about 30% and 70% of the tissue 14C at 2 and 10 min respectively. During the whole experimental period the specific radioactivity of glutamine was about three times higher than that of glutamate. Thus exogenous (14C)succinate elicited signs of metabolic compartmentation similar to those seen after the administration of short chain fatty acids or amino acids. Incorporation of 14C into gamma-aminobutyric acid (GABA) was very low after the injection of (1,4-14C)succinate. Since the oxidation of (1,4-14C)succinate via the cycle yields unlabelled GABA, whereas the reversal of the reactions in the GABA bypath may introduce 14C from succinate into the GABA pool, the results indicate that this reversal is negligible even under the most favorable conditions. 16 references. (Author abstract modified)

210782 Christensen, S. Department of Pharmacology, University of Copenhagen, Copenhagen, Denmark **Accumulation of lithium in the particulate fraction of rat brain following its long-term administration.** Journal of Neurochemistry (Oxford). 23(6):1299-1301, 1974.

The accumulation of lithium in the particulate fraction of the rat brain was examined after long-term administration. Lithium was found to cause significant accumulation in brain homogenate particles but had no effect on the concentrations of monovalent cations. This accumulation is thought to reflect either binding of lithium within subcelluar particles or maintenance of the high concentration of free lithium in cytoplasm entrapped within semi-intact neurons or synaptosomes or both. The lower accumulation of lithium in the liver indicates that the binding of lithium in the brain is due to specific brain tissue components. 10 references.

210787 Morishita, H.; Furukawa, T. Department of Pharmacology, Fukuoka University, Fukuoka, Japan **Possible mechanisms involved in the depressor response to dopamine.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 212(2):317-327, 1974.

Possible mechanisms involved in the depressor action of dopamine were studied using blood pressure recordings and isolated arterial strips in the rabbit. Dopamine elicited a purely depressor response. This depressor response to dopamine was reversed to a pressor response after blood pressure was lowered by pretreatment with hexamethonium, while dopamine induced a depressor response when blood pressure was lowered by infusion with acetylcholine or isoprenaline, or by pretreatment with sodium nitrite or bleeding. Dopamine elicited a dose dependent relaxing response in dog renal and mesenteric arterial strips contracted previously by potassium chloride after pretreatment with phenoxybenzamine or in rabbit aortic strips contracted previously by noradrenaline without phenoxybenzamine pretreatment. These relaxing responses were inhibited strongly by propranolol but were not affected by apomorphine. It is suggested that the ganglionic blocking and beta like effects of dopamine are involved in the depressor response to dopamine. 20 references. (Author abstract)

210788 Lindenbaum, A.; Marcher, K.; Wepierre, J.; Cohen, Y. Laboratoire de Pharmacodynamie, Universite de Paris-Sud, Rue Jean-Baptiste Clement, 92290 Chatenay-Malabry, France **/Blood-brain barrier: I. kinetics of distribution of 3H amphetamine in the rat brain after intravenous administration./** Barriere hemato-encephalique: I. cinetique de distribution de l'amphetamine 3H dans les structures du cerveau de rat apres administration intraveineuse. Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 212(2):337-347, 1974.

The kinetics of distribution through the rat brain following the intravenous administration of 3H-amphetamine was studied. Intravenously injected amphetamine penetrates rapidly in the brain, the cerebral spinal fluid and muscular tissues. Five minutes after the injection, the tissue to plasma concentration ratios (T/P) for brain, muscular tissues and cerebral spinal fluid amount to 5.7, 1.4and 0.8respectively. From 14 minutes on, the T/P ratio for muscle and cerebral spinal fluid remains constant and about equal to 1 and 3 respectively. Such an equilibrium between tissues and plasma concentration is not observed for the brain. The T/P ratio, equal to 10, 30 minutes after the injection, decreases significantly after that period and points to a slight fixation of the amine in this tissue. The evolution of the amphetamine concentration in the various brain areas reveals that the disimpregnation of the brain comes from white matter and that the amine is more strongly fixed by the grey structures. 13 references. (Journal abstract)

210789 Bramwell, G. J. Department of Pharmacology, School of Pharmacy, 29/39, Brunswick Square, London WC1N 1AX, England **The effect of antidepressants on unit activity in the midbrain raphe of rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 211(1):24-33, 1974.

The effect of imipramine, desipramine and pharmacologically related compounds on the activity of 5-hydroxytryptamine (5-HT) containing neurons were compared. Serotonergic neuron activity was monitored by recording the spontaneous single unit activity in the nucleus dorsalis raphe of chloral hydrate anesthetized rats. Imipramine, chlorpheniramine and p-chlormethylamphetamide (p-CMA) inhibited raphe unit firing, whereas desipramine, d-amphetamine and pargyline also excited some units. The relative potencies of the drugs as inhibitors of raphe unit firing roughly corresponded with their relative potencies as blockers of 5-HT reuptake and their ability to reduce brain 5-HT turnover. The possibility is discussed that excitation of raphe neuron activity by these drugs is caused by activation of excitatory noradrenaline (NA) inputs, whereas both 5-HT and NA terminals contribute towards neuronal inhibition. 31 references. (Author abstract)

210791 Allain, P.; Leblondel, G.; Diard, J.; Premel-Cabic, A.; Cailleux, A. Laboratoire de Pharmacologie C.H.U., 49036, Angers, France **/The effects of rubidium on the duration of sleep elicited by pentobarbital in the rat./** Influence du rubidium sur

la duree du sommeil provoque par le pentobarbital chez la souris. Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 211(1):159-164, 1974.

The influence of rubidium on the duration of sleep elicited by pentobarbital was examined in the rat. Swiss mice were given as the only source of drinking water a solution containing 0.05 or 0.025M of rubidium during 2, 5 or 10 days. In mice taking rubidium, the duration of pentobarbital sleeping time is significantly reduced. The sleeping time decreases when the duration of rubidium administration and the cerebral concentration of rubidium increase. The metabolism of pentobarbital is not enhanced and the animals awake with a cerebral concentration of rubidium equal or higher than in the control group. Weight gain and food intake are lower than in the control group. It is suggested that the pharmacological properties of rubidium have some similarities with those of amphetamine. 9 references. (Author abstract)

210792 Robichaud, R. C.; Goldberg, M. E. Department of Pharmacodynamics, Warner-Lambert Research Institute, Morris Plains, NJ 07950 **Pharmacological properties of two chlordiazepoxide metabolites following microsomal enzyme inhibition.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 211(1):165-173, 1974.

The demethylated (DCDP) and deaminated (Demoxepam) metabolites of chlordiazepoxide (CDP) and CDP itself were compared in several pharmacologic procedures with or without microsomal enzyme inhibition by SKF-525A. Only CDP showed any muscle relaxant properties, and this activity was unaltered by SKF-525A. DCDP was inactive in every procedure except in the punishment discrimination test in which all three compounds were active and all potentiated by SKF-525A. CDP and Demoxepam were equiactive in preventing either metrazol or electroshock convulsions, but the effect was potentiated only in the electroshock procedure. Finally, CDP prevented foot shock fighting in mice and rats but Demoxepam was active only in the mouse. These studies indicate that the antianxiety effect of CDP may be attributable to its demethylated metabolite, but that the muscle relaxant properties are inherent to CDP itself. The deaminated product appears to be metabolized differently in the rat than in the mouse. 12 references. (Author abstract)

210793 Bass, E.; Shani, J.; Givant, Y.; Yagil, R.; Sulman, F. G.; Berlin, C.; Foltyn, E.; Gordin, S.; Van Ham, I. Department of Applied Pharmacology, School of Pharmacy, Hebrew University, Jerusalem, Israel **The effect of psychopharmacologic prolactin releasers on lactation in sheep.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 211(1):188-192, 1974.

The effects of psychopharmacologic drugs on 14 prolactin releasers were studied in 59 lactating ewes during the fourth month of lactation, when milk yield had fallen to less than 50%, thus indicating lack of endogenous prolactin. Sum-3170, reserpine, piperacetazine, perphanazine, thiopropazate, propericiazine, P-4657-B, haloperidol, HF-2159, trifluperidol, tetrabenazine, perphenazine sulfoxide, aminopromazine, and SU-10704 were injected i.m. or i.v. for 6 consecutive days in doses of 0.005mg/kg-2.0mg/kg day. Daily measuring of milk yield showed that the following five substances increased declining lactation in drying up ewes: trifluperidol, Sum-3170, piperacetazine, P-4657-B, and perphenazine sulfoxide. This effect appeared only during the 6 day period of injection and then faded. It did not appear in 27 controls, it appeared, however, in crossover experiments. 12 references. (Author abstract)

210796 Garelis, E.; Young, S. N.; Lal, S.; Sourkes, T. L. Corfu Mental Hospital, Corfu, Greece **Monoamine metabolites in lumbar CSF: the question of their origin in relation to clinical studies.** Brain Research (Amsterdam). 79(1):1-9, 1974.

The sources of homovanillic acid (HVA), 3-methoxy-4-hydroxyphenylethylene glycol (MHPG) and 5-hydroxyindoleacetic acid (5HIAA) in lumbar CSF of man are discussed. Although HVA in lumbar CSF is derived from the brain, and MHPG seems to be mainly from the spinal cord, the origin of 5HIAA is uncertain. The evidence for and against a brain contribution to 5HIAA of the lumbar CSF is evaluated. It is concluded that the brain can contribute 5HIAA to 5HIAA to lumbar CSF under some circumstances. Measurement of 5HIAA concentrations in lumbar CSF can be of clinical value in detecting changes of 5-hydroxytryptamine (5HT) metabolism in the CNS if the changes are general throughout the CNS. 46 references. (Author abstract)

210800 Thierry, A. M.; Hirsch, J. C.; Tassin, J. P.; Blanc, G.; Glowinski, J. Groupe NB (INSERM U.114), College de France, 75005 Paris, France **Presence of dopaminergic terminals and absence of dopaminergic cell bodies in the cerebral cortex of the cat.** Brain Research (Amsterdam). 79(1):77-88, 1974.

Dopamine (DA) and noradrenaline (NA) levels were estimated in the suprasylvian gyrus and the cerebellum of the cat and compared to those found in the cerebral and cerebellar cortex of the rat. As in the rat, DA was undetectable in the cerebellum and represented about 30% of the total catecholamine (CA) levels in the cerebral cortex of the cat. The uptake of (3H)DA was estimated in homogenates of the suprasylvian cortex, the caudate nucleus and the cerebellum of the cat. In the suprasylvian cortex the (3H)-amine uptake was partially reduced by desipramine alone or benztropine alone and more extensively inhibited in the presence of both inhibitors. The synthesis of (3H)CA from (3H)tyrosine was estimated in slices of the suprasylvian gyrus and of the cerebellar cortex of the cat and was compared to that obtained in cerebral and cerebellar slices of the rat. In both species, the (3H)DA/(3H)NA ratio was higher in the cerebral cortex than in the cerebellum. 25 references. (Author abstract modified)

210801 Murthy, K. S. K.; Deshpande, S. S. Department of Surgery, University of Arizona Medical Center, Tuscon, AZ 85724 **Differential sensitivity of primary and secondary spindle afferents to depressant drugs.** Brain Research (Amsterdam). 79(1):89-99, 1974.

Intraarterial injections of capsaicin and benzonatate (Tessalon) were used to demonstrate the differential senstivity of primary and secondary spindle endings to depressant drugs. Capsaicin causes initial stimulation in both types of ending followed by a stage of depression. The primary endings are depressed first and recover later than the secondary endings. At least the depressant phase of capsaicin response appears to be due to direct action on the sensory endings. Tessalon causes immediate depression of the receptors with the primary endings again being more senstive. These effects are contrary to the local anaethetic action of Tessalon on nerve fibres. Desensitization to subsequent doses is prominent with capsaicin but not with Tessalon. Greater sensitivity of primary endings to excitatory drugs has already been well established. 28 references. (Author abstract modified)

210803 Tohyama, Masaya; Maeda, Toshiro; Shimizu, Nobuo. Department of Neuroanatomy, Institute of HIgher Nervous Activity, Osaka University Medical School, Osaka, Japan

Detailed noradrenaline pathways of locus coeruleus neuron to the cerebral cortex with the use of 5-hydroxydopa. Brain Research (Amsterdam). 79(1):139-144, 1974.

The detailed noradrenaline (NA) pathways of locus coeruleus (LC) neuron in the cerebral cortex of the rat were examined with the use of 6-hydroxydopa (6-OHD). Six hours after administration of 6-OHD delicate accumulation of the fluorescent substance is seen in the entire trajectory of the dorsal NA bundle except for terminal axons, which is traceable exclusively to the region of LC. The ascending fluorescent fibers form a compact bundle as the dorsal NA bundle and pass through the mesencephalon. At the midlevel of the lateral hypothalamus, a fiber bundle situated dorsally turns laterally and transverses the ventral part of the lentiform nucleus to reach the external capsule. The presence of three entries to the cerebral cortex of the dorsal NA bundle were demonstrated. 12 references.

210804 Simpson, John B.; Routtenberg, Aryeh. Department of Biology, University of Pennsylvania, Philadelphia, PA 19174 **Subfornical organ: acetylcholine application elicits drinking.** Brain Research (Amsterdam). 79(1):157-164, 1974.

The effects of increasing endogenous acetylcholine levels by topical application of anticholinesterase and the putative endogenous transmitter, acetylcholine, on the subfornical organ (SFO) of hte rat were examined. Both drugs produced short latency and short duration drinking behavior. The results suggest a possible cholinoceptive mechanism with the SFO which is involved in the control of drinking behavior. 20 references.

210806 Kluge, H.; Groschel, W.; Hartmann, W.; Zahlten, W.; Wieczorek, V. Klinik fur Psychiatrie un Neurologie "Hans Berger" der Friedrich-Schiller-Universitat, Jena, Germany **/Binding of lithium and calcium by cerebral membrane fractions.** Adsorption von Lithium - und Kalziumionen an zerebrale Membranfraktionen. Pharmakopsychiatrie Neuro Psychopharmakologie (Stuttgart). 7(6):293-299, 1974.

The absorption of lithium and calcium ions by cerebral microsomes and membranes from crude mitochondria after hypsoosmotic shock was examined. A binding of lithium to membranes of the shocked crude mitochondrial fraction could not be demonstrated under our experimental conditions. However, calcium was absorbed by this fraction in amounts of 0.7micro moles per 10mg of protein. Concentrations of 1mM calcium or higher prevented the binding of lithium to microsomes completely, while 1.5mM lithium lowered the binding capacity for calcium by 10-25% only. 12 references. (Author abstract modified)

210812 O'Callaghan, Michael A.; Duggan, P. Finbarr. Department of Biochemistry, University College, Cork, Ireland **Differential effects of chlorpromazine and chlorpromazine free radical on calcium transport in sarcoplasmic reticulum vesicles.** Biochemical Pharmacology (Oxford). 24(5):563-566, 1975.

The differential effects of chlorpromazine and chlorpromazine free radical on calcium transport in sarcoplasmic reticulum vesicles are described. Chlorpromazine activates, and chlorpromazine free radical inhibits, the calcium transport system of fragmented sarcoplasmic reticulum. The associated calcium dependent AT Pase is affected in a similar manner. The calcium independent (basal) ATPase is not reduced in activity by the free radical. It is suggested that unmodified chlorpromazine rather than its free radical form is the pharmacologically active moiety. 29 references. (Author abstract)

210813 Demisch, Lothar; Seiler, Nikolaus. Max-Planck Institut fur Hirnforschung, Arbeitsgruppe Neurochemie, Frankfurt, Germany **Oxidative metabolism of mescaline in the central nervous system -- V. In vitro deamination of mescaline to 3,4,5-trimethoxy-benzoic acid.** Biochemical Pharmacology (Oxford). 24(5):575-580, 1975.

The oxidative metabolism of mescaline in the central nervous system was studied. 3,4,5-Trimethoxy-benzoic acid (3,4,5-TMBA) besides 3,4,5-trimethoxy-phenylacetic acid (3,4,5-TMPAA) is formed from mescaline during its incubation with preparations of different mouse tissues. Brain has the highest capacity to form 3,4,5-TMBA among the tissues so far studied. The enzyme system which catalyses the oxidative deamination of mescaline to 3,4,5-TMBA is localized in the nuclear and microsomal fractions of brain. Oxygen, NAD(P)H and unidentified factors of the high speed supernatant of brain extract are necessary for optimal reaction conditions. 3,4,5-TMBA formation was inhibited by SKF 525-A, but not by MAO and DAO inhibitors. The similarities and dissimilarities of the enzymic deamination of amphetamine and mescaline are discussed. 36 references. (Author abstract)

210814 Gianutsos, Gerald; Hynes, Martin D.; Lal, Harbans. Department of Pharmacology and Toxicology, College of Pharmacy, University of Rhode Island, Kingston, RI 02881 **Enhancement of apomorphine-induced inhibition of striatal dopamine-turnover following chornic haloperidol.** Biochemical Pharmacology (Oxford). 24(5):581-582, 1975.

The enhancement of apomorphine induced inhibition of striatal dopamine turnover following chronic haloperidol is described. Following chronic treatment with haloperidol, there was no change in dopamine concentration or turnover in the rat striatum. However, the threshold dose of apomorphine to inhibit dopamine turnover was reduced. These data provide neurochemical evidence for supersensitivity of dopamine receptors after chronic treatment with neuroleptics. 18 references. (Author abstract)

210816 Kuczenski, R.; Segal, D. S.; Mandell, A. J. Pharmacology Department, Vanderbilt University, Nashville, TN **Regional and subcellular distribution and kinetic properties of rat brain choline acetyltransferase -- some functional considerations.** Journal of Neurochemistry (Oxford). 24(1):39-45, 1975.

The kinetic properties of soluble and membrane bound choline acetyltransferase (ChAc) were determined as a function of homogenization media and solubilization procedure in various regions of rat brain. The absolute levels and subcellular distribution of ChAc were determined in 11 brain regions to localize cholinergic cell bodies and nerve endings. Levels of ChAc varied from 139 munits/gtissue in caudate - putamen to 5-7 units/g tissue in cerebellum. The fraction of ChAc activity associated with synaptosomes varied from near 75% in caudate - putamen, hippocampus and cortical regions to near 20% in septum, locus coeruleus area and substantia nigra area. The apparent parallel distribution of cholinergic and catecholaminergic nerve endings is discussed in terms of a hypothetical model for the pathophysiology and treatment of Parkinson's syndrome. 45 references. (Author abstract modified)

210818 Roufogalis, B. D. Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, British Columbia, V6T 1W5 **Comparative studies on the membrane actions of depressant drugs: the role of lipophilicity in inhibition of brain sodium and potassium-stimulated ATPase.** Journal of Neurochemistry (Oxford). 24(1):51-61, 1975.

A correlation was found between lipid solubility and potency of various local anaesthetics, antihistamines, tricyclic antidepressants and phenothiazine tranquilizers as inhibitors of the sodium potassium (Na-K) ATPase activity of a microsomal membrane fraction from bovine brain cortex. Depressant drugs such as chlorpromazine, which have the greatest lipid solubilities were competitive inhibitors of Na activation but noncompetitive toward K activation, whereas drugs such as tetracaine with lower lipid solubilities were competitive inhibitors of K activation but noncompetitive toward Na activation. These data suggest that the more lipid soluble phenothiazines penetrate into and react in hydrophobic areas of the membrane microenvironment resulting in a membrane perturbation which interferes with Na activation. On the other hand the less lipid soluble local anaesthetics probably act at superficial sites near the membrane surface resulting in a different membrane perturbation which interferes with the K activation mechanism. 42 references. (Author abstract modified)

210819 Gal, E. M.; Christiansen, P. A. Department of Psychiatry, University of Iowa, Iowa City, IA 52242 **Alpha-methyltyrptophan: effects on cerebral monooxygenases in vitro and in vivo.** Journal of Neurochemistry (Oxford). 24(1):89-95, 1975.

The effects of alpha-methyltryptophan (AMTP) on cerebral monooxygenases in vitro and in vivo were examined in the rat. Following administration of AMTP there was a time dependent decrease of serotonin and a concomitant increase of methyl-5-hydroxy-tryptamine (AM-5-HT) in most cerebral areas. AMTP is hydroxylated to alpha-methyl-5-hydroxytryptophan (AM-5-HTP) by cerebral tryptophan hydroxylase in vitro and in vivo. Hydroxylation of AMTP in vitro and in vivo was markedly inhibited in p-chlorophenylalanine (p-CP) treated rats. After administration of AMTP, the conversion in vivo of tyrosine to norepinephrine was inhibited. This inhibition was not apparent in p-CP pretreated animals. p-Chloroamphetamine (p-CA) lowered serotonin and AM-5-HT levels in some areas of the brain but unlike p-CP alone or in combination with AMTP it did not significantly inhibit hydroxylation of tryptophan. 29 references. (Author abstract modified)

210820 Rosenthal, M.; LaManna, J. C. Department of Physiology and Pharmacology, Duke University, Durham, NC 27710 **Effect of ouabain and phenobarbital on the kinetics of cortical metabolic transients associated with evoked potentials.** Journal of Neurochemistry (Oxford). 24(1):111-116, 1975.

The effects of ouabain and phenobarbital on the kinetics of cortical metabolic transients asssociated with evoked potentials were examined. Ouabain introduced directly under the cortical surface, markedly slowed the on kinetics with no change in recovery metabolism. Phenobarbital delays the reduction of NAD+ (off kinetics) with little effect on on kinetics. Thus, the transient fluorometric response to evoked potentials is confirmed as a measure of ATP breakdown and oxidative rephosphorylation. The rate of NADH oxidation is a measure of the rising ADP concentration due to the action of the Na-K ATPase. The rate of return of the fluorescence to baseline levels (reduction of NADH) is a function of the respiratory chain. 33 references. (Author abstract modified)

210821 Stolk, J. M. Department of Psychiatry, Dartmouth Medical School, Hanover, NH 03755 **Evidence for reversible inhibition of brain dopamine-beta-hydroxylase activity in vivo by amphetamine analogues.** Journal of Neurochemistry (Oxford). 24(1):135-142, 1975.

Evidence of the reversible inhibition of dopamine-beta-hydroxylase (DBH) activity by amphetamine to in the rat is reported. Rats treated with D-amphetamine have a decreased ability to convert intracisternally injected radioactive dopamine to noradrenaline. This effect is dose related and reversible by increasing the dose of injected dopamine. L-Amphetamine is equipotent to the D-isomer, but para-hydroxyamphetamine reduces noradrenaline formation only slightly. Like the amphetamines, imipramine produces significant inhibition of noradrenaline from labelled dopamine, however, dopamine content after imipramine, but not after the amphetamines was consistently decreased. The divergent effects of the amphetamine and imipramine on noradrenaline accumulation from labelled tyrosine suggest that the amphetamines' effect on in vivo (DBH) activity are not solely attributable to interference with transport and, therefore, suggest a direct effect on the enzyme. 24 references. (Author abstract modified)

210825 Kuczenski, Ronald. Tennessee Neuropsychiatric Institute, Pharmacology Dept., Vanderbilt University, Nashville, TN **Effects of catecholamine relasing agents on synaptosomal dopamine biosynthesis: multiple pools of dopamine or multiple forms of tyrosine hydroxylase?** Neuropharmacology (Oxford). 14(1):1-10, 1975.

The effects of agents, which are known to induce release of catecholamines from synaptosomes were assessed on the synthesis of dopamine from tyrosine, as reflected in the evolution of 14CO2 from L-(1-14C)-tyrosine, in intact rat striatal synaptosomes. Neither reserpine, tyramine, nor amphetamine effected the activity of tyrosine hydroxylase or DOPA decarboxylase in the absence of synaptosomal structural integrity. Nor did these drugs affect the accumulation of (3H)-tyrosine into synaptosomes. The data are consistent with the existence of at least two pools of synaptosomal dopamine, one of which can interact with tyrosine hydroxylase. The rate of dopamine synthesis in synaptosomes from amphetamine pretreated rats was assessed in the presence of reserpine and tyramine. The data are not consistent with alterations in pool size being the only mechanism affecting synaptosomal dopamine synthesis. A mechanism is discussed involving an equilbrium of tyrosine hydroxylase between active and inactive conformers in the presence of an inhibitory pool of dopamine. 30 references. (Author abstract modified)

210826 Gal, E. M.; Christiansen, P. A.; Yunger, L. M. Neurochemical Research Laboratory, Department of Psychiatry, University of Iowa, Iowa City, IA 52242 **Effect of p-chloroamphetamine on cerebral tryptophan-5-hydroxylase in vivo: a reexamination.** Neuropharmacology (Oxford). 14(1):31-39, 1975.

A hypothetical reaction sequence for the synthesis of a metabolite from para-chloroamphetamine (p-CA) is proposed. p-CA exerts two distinct effects: a short-term one lasting 48 hr and a long-term one responsible for the progressive decrease in levels of serotonin (5-HT) and in hydroxylation of tryptophan. In two weeks there was a 40% concurrent reduction in the in the hydroxylation of tryptophan in the Vmax of tryptophan hydroxylase from brainstem, in the recovery of the total enzyme units and in the turnover rate of 5-HT. The uptake of (3H)-5-HT by synaptosomal fractions from various areas of the brain at 3 and 14 days after p-CA treatment revealed marked impairment in the high affinity uptake. This did not occur 3 days after administration of p-chlorophenylalanine. These changes are interpreted as the outcome of neurotoxicity brought about by a metabolite of p-CA which

would specifically affect the serotoninergic system. A hypothetical scheme for the biological synthesis of such a metabolite is given. 30 references. (Authro abstract modified)

210827 Key, B. J. Department of Pharmacology, Medical School, University of Birmingham, Birminigham B15 2TJ, England **Electrocortical changes induced by perfusion of catecholamines into the brainstem reticular formation.** Neuropharmacology (Oxford). 14(1):41-51, 1975.

Electrocortical changes induced by perfusion of catecholamines into the brainstem reticular formation were examined. Various concentrations of noradernaline and related catecholamines were perfused bilaterally into the pontine and mesencephalic reticular formation using push pull cannulae. The initial effect of a 5 min perfusion of (-)-noradrenaline, (-)-adrenaline, (-)-phenylephrine or alpha-menthyl noradrenaline, was to induce a two stage change in the electrocortical activity, that is phasic followed by tonic desynchronisation. Using tritium labelled (+ or -)-(7-3H)-noradrenaline, it was established that the total amount of drug diffisuing into the brain tissue was very low. The appearance of phasic electrocortical changes correlated with 0.4-25 ng noradrenaline (base) within the brain at the end of each cannula. Tonic electrocortical desynchronization gave tissue levels of exogenous noradrenaline (base) of 6.5-103ng. Secondary sedative effects were usually observed with tissue levels in excess of 98ng at the end of each cannula. 48 references. (Author abstract modified)

210828 Freemon, Frank R.; Rosenbaltt, Jack E.; El-Yousef, M. Khaled. Neurology Service, Nashville VA Hospital, Nashville, TN **Interaction of physostigmine and delta-9-tetrahydrocannabinol in man.** Clinical Pharmacology and Therapeutics. 17(2):121-126, 1975.

To investigate the hypothesis that delta-9-tetrahydrocannabinol (THC), the major psychoactive ingredient of marihuana, acts by interfering with cholinergic brain mechanisms, 0.75 to 1.25mg of physostigmine, a centrally active cholinergic drug, was given intravenously to five normal volunteers who had ingested 20 to 40mg of THC 2 hours earlier. Physostigmine decreased the degree of tachycardia and conjunctival injection produced by THC. The major psychologic effects of physostigmine were amplification of the lethargy and somnolence which occur late in the course of THC intoxication. The lack of physostigmine counteraction of the peak psychologic effects of THC was interpreted as evidence against the hypothesis that THC acts predominantly by an anticholinergic mechanism. 12 references. (Author abstract)

210830 Hendley, Edith D.; Welch, Bruce L. Department of Physiology and Biophysics, University of Vermont, College of Medicine, Burlington, VT 05401 **Electroconvulsive shock: sustained decrease in norepinephrine uptake affinity in a reserpine model of depression.** Life Sciences (Oxford). 16(1):45-54, 1975.

The effect of electroconvulsive shock given once daily for nine consecutive days to chronically reserpinized mice was examined. Shocked mice explored more actively than controls in an open field 18-20 hours after the last shock, suggesting a reversal of reserpine depression. The apparent Km for the high-affinity active uptake of norepinephrine into crude synaptosome rich homogenates of their cerebral cortices lowered affinity for norepinephrine uptake. The Vmax for norepinephrine uptake was also elevated, suggesting that the number of uptake sites had increased as well. 24 references. (Author abstract)

210831 Rommelspacher, Hans; Kuhar, Michael J. Department of Pharmacology and Experimental Therapeutics, The Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Effects of dopaminergic drugs and acute medial forebrain bundle lesions on striatal acetylcholine levels.** Life Sciences (Oxford). 16(1):65-70, 1975.

The effects of dopaminergic drugs and acute medial forebrain bundle lesions on striatal acethylcholine levels were examined. Placement of radio frequency lesions in the medial forebrain bundle resulted in a 50% depletion of striatal acetylcholine levels but did not change hippocampal levels. A similar result was obtained with the administration of chlorpromazine, haloperidol and pimozide. When these drugs were administered simultaneously with placement of lesions, there was the same 50% depletion of striatal acetylcholine. Apomorphine reversed the depletion due to lesions. These results suggest that the action of antipsychotic drugs on the cholinergic system in the striatum is primarily due to their action at dopamine receptors rather than a direct action on cholinergic receptors which would be due to their anticholinergic activity. 22 references. (Author abstract)

210834 Gram, Lars F.; Christiansen, Johannes; Overo, KerstinFredrickson. Psychochemistry Institute, Copenhagen, Denmark **Pharmacokinetic interaction between neuroleptics and tricyclic antidepressants in the rat.** Acta Pharmacologica et Toxicologica (Kobenhavn). 35(3):223-232, 1975.

The metabolism and disposition of 14C-nortriptyline and 14C-imipramine in the rat was studied after intraperitoneal administration of single doses of the drug. With 14C-nortriptyline, it was found that concomitant administration of perphenazine caused a rise in plasma level and tissue concentration of unchanged nortriptyline. WIth 14C-imipramine, it was found that administration of perphenazine caused an increase in tissue concentration of imipramine, desipramine, and iminodibenzyl. At the same time total excretion by the feces and the urinary excretion of imipramine-N-oxide was increased in perphenazine pretreated rats. These results indicate that perphenazine in rats inhibits the hydroxylation and/or glucuronide formation of imipramine, whereas demethylation, N-oxidation, and dealkylation seem to be unaffected. Dose response studies showed that perphenazine and chlorpromazine have equivalent potency with regard to the increased tissue concentration of 14C-imipramine. 12 references. (Author abstract)

210850 Sloan, J. W.; Martin, W. R.; Clements, T. H.; Buchwald, W. F.; Bridges, S. R. National Institute on Drug Abuse, Addiction Research Center, Lexington, KY 40511 **Factors influencing brain and tissue levels of tryptamine: species, drugs and lesions.** Journal of Neurochemistry (Oxford). 24(3):523-532, 1975.

In a study of the factors influencing brain and tissue levels of tryptamine, brain tryptamine levels in the rat and guinea pig were found to be less than those in the dog and cat. Regional distribution studies in the dog and cat showed that tryptamine was present in all major brain regions with highest concentrations in the spinal cord. Blood levels of tryptamine in the guinea pig, dog and cat; were lower than brain levels. Pargyline significantly increased brain tryptamine in both the dog and cat; whereas isocarboxazid increased brain tryptamine levels in dog but decreased levels in the cat. Reserpine did not significantly decrease brain, spinal cord or blood tryptamine levels in the dog. Spinal cord transection did not decrease tryptamine levels below the lesion in the chronic spinal dog. 4 references. (Author abstract modified)

210855 Yehuda, Shlomo; Wurtman, Richard J. Department of Psychology, Bar-Ilan University, Ramat-Gan, Israel **Dopaminergic neurons in the nigro-striatal and mesolimbic pathways: mediation of specific effects of d-amphetamine.** European Journal of Pharmacology (Amsterdam). 30(2):154-158, 1975.

In a study of dopaminergic neurons in the nigro striatal and mesolimbic pathways, the administration of d-amphetamine to rats caused stereotypy, hypothermia among animals placed in a cold environment, and paradoxical behavioral thermoregulation (i.e.,animals in a cold environment choose not to place themselves under the beam emitted by a heat lamp). These effects were blocked in animals lesioned unilaterally in the mesolimbic dopaminergic projections to the olfactory tubercule and nucleus accumbens. In contrast, a unilateral lesion destroying the nigro striatal projections within the caudate nucleus blocked none of these responses, and actually potentiated the induction of stereotypy by d-amphetamine. Both lesions cause the animal to exhibit rotational behavior in response to the subsequent administration of d-amphetamine. These observations suggest that the mesolimbic dopaminergic projections mediate some of the behavioral and visceral effects of d-amphetamine. 11 references. (Author abstract)

210856 Karobath, Manfred E. Department of Experimental Psychiatry, Psychiatrische Universitatsklinik, Universitat Wien, Vienna, Austria **Tricyclic antidepressive drugs and dopamine-sensitive adenylate cyclase from rat brain striatum.** European Journal of Pharmacology (Amsterdam). 30(2):159-163, 1975.

Tricyclic antidepressant drugs examined as inhibitors of dopamine sensitive adenylate cyclase in a cell-free homogenate of rat brain striatum. Amitriptyline and doxepin were found to be potent inhibitors of dopamine sensitive adenylate cyclase, chlorimipramine and nortriptyline were moderate inhibitors and imipramine, desmethylimipramine, protriptyline and melitracene were weak inhibitors. 13 references. (Author abstract)

210857 Corrodi, Hans; Farnebo, Lars-Ove; Fuxe, Kjell; Hamberger, Bertil. no address **Effect of ergot drugs on central 5-hydroxytryptamine neurons: evidence for 5-hydroxytryptamine release or 5-hydroxytryptamine receptor stimulation.** European Journal of Pharmacology (Amsterdam). 30(2):172-181, 1975.

The effects of ergot drugs on 5-hydroxytryptamine (5-HT) receptor activity were evaluated using the extensor hindlimb reflex of acutely spinalized rats. It was found that ergocornine increased the 5-HT receptor activity independent of presynaptic 5-HT stores and that it did not have any effects on uptake, retention and spontaneous overflow of 3H-5-HT in vitro but reduced the field stimulation induced release of 3H-5-HT in vitro. It is suggested that ergocornine is a 5-HT receptor stimulating agent, an effect which may lead to reduction of nervous impulse flow in the 5-HT neurons and subsequently of 5-HT release and turnover. It is suggested that the ergolene derivative PTR 17402 (MPME) is a releaser of extragranular 5-HT stores leading to increased 5-HT receptor activity and reduction of 5-HT turnover in the same way as indicated for ergocornine. This new ergolene derivative may represent a new class of antidepressant drugs acting via release of extragranular 5-HT stores. 34 references. (Author abstract modified)

210858 Tuomisto, Jouko; Ranta, Tapio; Mannisto, Pekka; Saarinen, Ari; Leppaluoto, Juhani. Department of Pharmacology, University of Helsinki, Helsinki, Finland **Neurotransmitter control of thyrotropin secretion in the rat.** European Journal of Pharmacology (Amsterdam). 30(2):221-229, 1975.

Neurotransmitter control of thyrotropin secretion in the rat was examined. In rats adapted to a +30 degree C temperature for 1 week, transfer to a temperature of +4 degrees C increased immunoassayable serum thyroid stimulating hormone (TSH). Since this response, as well as the level of serum TSH without stimulation, were decreased by reserpine, phentolamine, phenoxybenzamine, disulfiram and diethyldithiocarbamate, noradrenaline may be involved in the stimulation of TSH secretion. L-Dopa, a noradrenaline precursor, decreased the TSH response to cold; alpha-methyl-p-tyrosine increased the TSH level. Apomorphine decreased the level of serum TSH and inhibited the response to cold. The possibility of a dopaminergic inhibitory factor released from the hypothalamus is discussed. 5-HT has possibly a role in the regulation of TSH secretion, since its precursor 5-HTP decreased the response to cold. No indication was found that acetylcholine is involved. 32 references. (Author abstract modified)

210859 Kuczenski, Ronald; Segal, David S. Tennessee Neuropsychiatric Institute, 1501 Murfreesboro Road, Nashville, TN 37217 **Differential effects of D- and L-amphetamine and methylphenidate on rat striatal dopamine biosynthesis.** European Journal of Pharmacology (Amsterdam). 30(2):244-251, 1975.

The differential effects of D-amphetamine and L-amphetamine and methylphenidate on rat striatal dopamine (DA) biosynthesis were examined. Methylphenidate and the optical isomers of amphetamine have differential effects, in vivo and in vitro on rat striatal synaptosomal DA biosynthesis. Whereas the systemic administration of D-amphetamine or L-amphetamine produces a dose dependent decrease in synaptosomal DA synthesis, methylphenidate, at doses which produce comparable degrees of stereotyped behavior, has no effect on this measure of DA biosynthesis. Although in vitro methylphenidate can partially activate DA synthesis, it does not overcome the resperine induced inhibition. The data are discussed in terms of the possible differential mechanisms by which these two types of stimulants may exert their effects on stereotypy. 32 references. (Author abstract modified)

210862 Shore, Parkhurst A.; Dorris, Roy L. Department of Pharmacology, University of Texas Health Science Center, Dallas, TX **On a prime role for newly synthesized dopamine in striatal function.** European Journal of Pharmacology (Amsterdam). 30(2):315-318, 1975.

A role for newly synthesized dopamine in striatal function is described. Rats were given either the tyrosine hydroxylase inhibitor, alpha-methyltyrosine (MT) or the neuroleptic, haloperidol. Other rats received both drugs (haloperidol 30 min after MT). This dose of haloperidol alone caused only a slight, gradually developing catalepsy, while MT alone caused none. The combination quickly caused a strong catalepsy. Striatal dopamine (DA) stores were only minimally depleted at the time of catalepsy potentiation. The marked elevation of striatal homovanillic acid concentration seen after haloperidol administration was greatly inhibited by MT pretreatment. It is concluded that the marked potentiation of haloperidol induced catalepsy by MT is related to the absence of newly synthesized DA rather than to an exhausted main DA pool and that newly synthesized DA has a greater role in striatal function than does DA of the main striatal storage pool. 12 references. (Author abstract)

210864 Wiesel, Frits-Axel; Sedvall, Goran. Department of Pharmacology, Korolinska Institutet, S-104 01, Stockholm,

Sweden **Effect of antipsychotic drugs on homovanillic acid levels in striatum and olfactory tubercle of the rat.** European Journal of Pharmacology (Amsterdam). 30(2):364-367, 1975.

Dose response curves for the elevation of homovanillic acid levels in corpus striatum and olfactory tubercle of rats were determined by mass fragmentography after treatment with antipsychotic drugs. The order of potency in both regions was: haloperidol, chlorpromazine, thioridazine and clozapine. The relative elevation of the content of homovanillic acid was significantly greater in the striatum than in the olfactory tubercle for all drugs except thioridazine. The antipsychotic effect of the drugs tested may be related to the interference with dopaminergic mechanisms in striatal and/or limbic areas. 13 references. (Author abstract)

210865 Johansson, Jan O.; Jarbe, Torbjorn U. C. University of Uppsala, Department of Psychology, Uppsala, Sweden **Diazepam as a discriminative cue: its antagnoism by bemegride.** European Journal of Pharmacology (Amsterdam). 30(2):372-375, 1975.

In a study of diazepam as a discriminative cue, Gerbils were trained to respond differentially to the presence of absence of diazepam in a T-maze. Ss showed a dose related antagonism when challenged with bemegride. Gerbils trained with a mixture of diazepam and bemegride evidenced response control more slowly than the group trained solely with diazepam. 5 references. (Author abstract)

210866 Kayaalp, S. O.; Kaymakcalan, S.; Verimer, T.; Ilhan, M.; Onur, R. Institute of Pharmacology and Toxicology, Hacettepe University, Ankara, Turkey **In vitro neuromuscular effects of delta9-tetrahydrocannabinol (THC).** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 212(1):67-75, 1974.

The effects of tetrahydrocannabinol (THC) were investigated on the twitch responses to indirect and direct stimulation of the muscle in the isolated rat phrenic nerve - diaphragma prepartion. THC induced an inital potentiation of both types of respones. At higher concentration it induced a slowly developing blockade of the responses to indirect stimulation and a slowly developing small contracture. The muscle recovered slowly and partly after washing THC out. When applied on a portion of the nerve rather than on the whole preparation it caused a partial conduction block in the nerve. THC induced block was not reversed by neostigmine. The data suggest that THC induced block of the responses to indirect stimulation may be due to the interference of this drug with the depolarization of the motor nerve fibers and their terminals. The drug also might interfere with the calcium pool of the skeletal muscle. 14 references. (Author abstract)

210869 Proctor, C. D.; Kirby, J.; Wood, M. H.; Wade, L. H.; King, P. K. Gillette Memorial Laboratory, Meharry Medical College, Nashville, TN 37208 **Comparison of the effects of d-amphetamine and l-amphetamine in reversing depression of mouse locomotor activity caused by reserpine.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 212(1):108-115, 1974.

The effect of dl-amphetamine, d-amphetamine and l-amphetamine in reversing the depression of quantitiatively measured locomotor activity produced in mice by reserpine was studied. It was found that dl-amphetamine was able to reverse the depression of locomotor activity produced by reserpine and that d-amphetamine, given in dosage equal to its contribution to effective dl-amphetamine dosage was also able to effect this reversal. L-amphetamine, given analogously to the d-amphetamine, was not effective in causing reversal of the reserpine action. The stimulation of mouse locomotor activity caused by dl-amphetamine and d-amphetamine in reserpinized mice was less than that caused by equal dosage of these agents in unreserpinized mice. Mice reserpinized to the same degree found to be reversed by the dl-amphetamine and d-amphetamine showed marked depletion of brain norepinephrine, dopamine and serotonin, irrespective of whether or not they had been also treated with d-amphetamine or l-amphetamine and whether or not these agents were capable of reversing reserpine induced depression of locomotor activity. 11 references. (Author abstract)

210872 Moniuszko-Jakoniuk, J.; Wisniewski, K.; Bodzenta, A. Department of Pharmacology, Medical School, Mickiewicza 2, 15-222 Bialystok, Poland **Effect of the activation of the kinin-forming system on the potency of chlorpromazine.** Pharmacology (Basel). 12(4-5):216-223, 1975.

The effects of the activation of the kinin forming system on the action of chlorpromazine in rats and mice was examined. It was found that in animals with central nervous system (CNS) kinin enzymes previously activated with kallikrein, or in animals which had been given bradykinin, the psychodepressive activity of chlorpromazine became markedly higher. The administration of Trasylol brought about a decrease of the postkallikrein activation of kinin-generating enzymes and abolished the potentiating kallikrein effect on the action of chlorpromazine. Under multiple pathological conditions which are followed by increased kinin levels, an altered potency of drugs acting on CNS should be taken into consideration. 21 references. (Author abstract)

210875 Leonard, B. E. Pharmacology Department, Organon Scientific Development Group, Oss, The Netherlands **The effect of two synthetic ACTH analogues on the metabolism of biogenic amines in the rat brain.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 207(2):242-253, 1974.

The effect of adrenocorticotropin hormone (ACTH) and ACTH (7-D-Phe) on brain serotonin, noradrenaline, dopamine, their amino precursors, gamma-aminobutyric acid and 5-hydroxyindoleacetic acid were studied in the rat following both acute and chronic administration. These peptides delay and potentiate respectively the extinction of a conditioned avoidance response. The most marked biochemical changes were found following chronic administration of the peptides. The effects were qualitatively similar. Both peptides reduced the concentration of gamma-aminobutyric acid and serotonin in the midbrain region, an area where other investigators consider the peptides have their main site of action. From synthesis inhibition studies, there is evidence that these peptides increase the turnover of noradrenaline and reduce that of serotonin. It is concluded that in the rat there does not appear to be a direct correlation between the effect of these peptides on brain amine metabolism and their opposing effects on the extinction of a conditioned avoidance response. 20 references. (Author abstract)

210876 Newman, L. M.; Lutz, M. P.; Domino, E. F. Department of Pharmacology, Wayne State University, School of Medicine, Detroit, MI 48207 **Delta9-tetrahydrocannabinol and some CNS depressants: evidence for cross-tolerance in the rat.** Archives Internationals de Pharmacodynamie et de Therapie (Ghent). 207(2):254-259, 1974.

In a study of cross-tolerance, rats trained in a one way shock avoidance situation were made tolerant to the depressant effects of delta9-tetrahydrocannabinol (THC) by giving the drug daily. Ethyl alcohol and pentobarbital did not greatly affect tolerant rats. Morphine, chlorpromazine and pentobarbital did significantly depress the behavior of tolerant and nontolerant rats in the avoidance situation. In addition, rats were trained to press on a F12 schedule for water reinforcement. These animals also showed tolerance to THC and cross-tolerance of ethyl alcohol. Larger doses of alcohol completely suppressed responding and hence no cross-tolerance to THC was observed. It was concluded that the cross-tolerance seen is due to the drugs themselves and limited to sedative - hypnotic agents in low doses. 3 references. (Author abstract)

210877 Hart, J. L. Department of Pharmacology, University of Hawaii, Honolulu, HI 96822 **Effects of hyperbaric conditions on the response of animals to central nervous system stimulants and depressants.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 207(2):260-269, 1974.

The effects of hyperbaric conditions on the responses of animals to central nervous system (CNS) stimulants and depressants were examined. Awakening times were observed in animals in normobaric and hyperbaric air following administration of the CNS depressant pentobarbital. Awakening times of mice following doses of 50 and 75mg/kg of pentobarbital were significantly longer at 2, 4, 6, and 8 than those at 1 ATA. However, hyperbaric conditions did not significantly alter the awakening times of cats, guinea pigs, or rats. In 6 ATA air, the LD50 for the CNS stimulant picrotoxin in mice was significantly increased more than twofold above that at 1 ATA; the LD50 for caffeine was unaffected. The protective effect of hyperbaric conditions was due to the elevated PO2, for if the PO2 was kept constant and the PN2 was increased, the LD50 for picrotoxin was unaltered. 11 references. (Author abstract)

210880 Kadzielawa, K. Department of Experimental Pharmacology, Academy of Medicine, Warsaw 00-927, ul. Krak. Przedm. 26/28, Poland **The EEG effects of Dopa in the rabbit depending upon the level of brain-stem section.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 207(2):310-321, 1974.

The electroencephalogram (EEG) effects of DOPA infused into the common carotid artery were analyzed in rabbits with different levels of brainstem section. In contrast to gallamine immobilized rabbits or encephale isole preparations, in which DOPA in doses below 10mg was unable to induce consistent and evident changes in the EEG pattern, this catecholamine precursor elicited profound effects, predominantly in the ipsilateral hemisphere, in the preparations with postpontine, rostropontine and intercollicular sections. The effect of DOPA consisted of a marked decrease of amplitude and a less pronounced increase in frequency from cortical areas and of theta rhythm in the ipsilateral hippocampys and caudate nucleus. It is concluded that DOPA induced activation in the rabbit is attenuated by the tonic ascending influences of the synchronizing bulbar structures. It is suggested, that the observed effects of DOPA are mainly dependent on the action of dopamine. 72 references. (Author abstract modified)

210881 Gogolak, G.; Huck, S.; Porges, P.; Stumpf, Ch. Department of Neuropharmacology, University of Vienna, Vienna, Austria **Action of strychnine and central depressants on the cerebello-rubral system.** Archive Internationales de Pharmacodynamie et de Therapie (Ghent). 207(2):322-332, 1974.

The actions of strychnine and hexobarbital or propanidid on the cerebello - rubral system of the rabbit were compared. Under the influence of any of these drugs high amplitude rhythms appear in both the cerebellum and the red nucleus and the red nucleus neurons fire in bursts correlated to the cerebello - rubral rhythm. Changes of the cerebello - rubral activity were always accompanied by corresponding changes of the firing pattern of red nucleus neurons. Differences in the amplitude, the range of the frequencies and the optimal frequencies of the cerebello - rubral rhythm as well as the burst firing pattern of the red nucleus neurons were found with strychnine when compared to hexobarbital and propanidid. The findings indicate that the similarities in the electrographic changes induced by strychnine and the barbiturate like agents are only superficial. 37 references. (Author abstract modified)

210883 Krell, Robert D.; Goldberg, Alan M. Johns Hopkins University, School of Hygiene and Public Health, Department of Environmental Medicine, Baltimore, MD 21205 **Effect of choline acetyltransferase inhibitors on mouse and guinea-pig brain choline and acetylcholine.** Biochemical Pharmacology (Oxford). 24(3):391-396, 1975.

The effects of two choline acetyltransferase (CAT) inhibitors, 4-(1-naphthylvinyl) pyridine (NVP) and 4-(3-chlorophenylvinyl) pyridine (3-chloro-4-stilbazole; CS) on mouse and guinea pig brain acetylcholine (ACh) and choline were examined. The intraperitoneal administration of NVP or CS appeared to inhibit CAT partially in both species, but both compounds were without effect on steady state levels of ACh. In the mouse CS, but not NVP, increased brain choline. Both CS and NVP were shown to reduce, but not totally inhibit, the synthesis of mouse brain ACh. The inability of these compounds to decrease steady state levels, while apparently decreasing synthesis rates, suggests that CAT may not be the rate limiting step in ACh synthesis. 17 references. (Author abstract)

210884 Rapin, J.; Jacquot, C.; Guedri, H. El.; Cohen, Y. Department of Pharmacology, F 92290 Chatenay-Malabry, France **Effects of amphetamine and its hydroxylated derivatives on newly synthesized hypothalamic norepinephrine; study in vitro.** Biochemical Pharmacology (Oxford). 24(3):428-429, 1975.

Evidence that newly synthesized norepinephrine is preferentially released in brain tissue of rats by both amphetamine and its metabolites is presented. In all cases the ratio of the specific radioactivity of the hypothalamic slices and that of the supernatant shows that there is a preferential release of newly synthesized norepinephrine. Despite these similarities, there are large differences in the mechanism of the three amines' activity. With both amphetamine and alpha-methyloctopamine there is a decrease in the specific radioactivity of tissue norepinephrine and an increase in the specific radioactivity of supernatant norepinephrine. It is partially masked by the more important release of endogenous transmitter, resulting from the granular penetration of the false transmitter. In the case of hydroxyamphetamine, there is an increase in the specific radioactivity of the norepinephrine in the supernatant, but there is no effect in the tissue. These apparently contradictory results can be explained by an accelerated synthesis of 3H-norepinephrine in the tissue. In conclusion, the three amines studied, having different mechanisms of activity, produce the same results, preferential release of newly synthesized norepinephrine. 13 references.

210887 Tessel, Richard E.; Woods, James H.; Counsell, Raymond E.; Basmadjian, G. P. Department of Pharmacology,

M6322 Medical Science Building, Medical School, University of Michigan, Ann Arbor, MI 48104 **Structure-activity relationships between meta-substituted N-ethylamphetamines and isolated guinea-pig atrial rate.** Journal of Pharmacology and Experimental Therapeutics. 192(2):319-326, 1975.

The effects of N-ethylamphetamines (NEAs) substituted at the meta position of the phenyl ring with H, F, Cl, Br, I, CF3, CH3O, NO2, or OH were examined on the rate of spontaneously beating isolated guinea pig atria. All compounds, with the exception of meta-iodo NEA and meta-trifluoromethyl NEA (fenfluramine), increased atrial rate to varying degrees, as determined in cumulative concentration-response curves that included concentrations which were ineffective through those which decreased rate. Analyses indicated that the respective maximum increases in atrial rate produced by these compounds were inversely related to the meta substituted steric factor (size); neither hydrophobic nor electronic substituent effects contributed significantly to the relationship. In atria obtained from guinea pigs pretreated with the monoamine oxidase inhibitor, pargyline, the stimulant effects of these compounds were markedly potentiated and were again inversely related only to substitutent size. The interactions of pargyline and reserpine pretreatment with the actions of these NEA congeners suggest that all are indirectly acting sympathomimetic amines, except the hydroxylated compound, which is mixed acting. 26 references. (Author abstract modified)

210888 Long, J. P.; Heintz, S.; Cannon, J. G.; Kim, J. Department of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52242 **Inhibition of the sympathetic nervous system by 5,6-dihydroxy-2-dimethylamino tetralin (M-7), apomorphine and dopamine.** Journal of Pharmacology and Experimental Therapeutics. 192(2):336-342, 1975.

The inhibition of the sympathetic nervous system by 5,6-dihydroxy-2-dimethylamino tetralin (M-7), apomorphine and dopamine was examined. M-7 reduces the resting heartrate of anesthetized dogs and cats and blocks reflex activation of the sympathetic nervous system. M-7 inhibites the response to postganglionic stimulation of the right cardioaccelerator nerve if the frequency of stimulation is 2 Hz; no inhibition is observed with a frequency of 18Hz. The inhibitory action of M-7 is antagonized by haloperidol or chlorpromazine. Similar inhibitory actions and frequency specificity were observed in vitro using the right atrium of the cat and nerve stimulation. In cats, nerve stimulation was inhibited by apomorphine. Dopamine, in the presence of cocaine, also inhibited low frequency nerve stimulation. It is postulated that prejunctional sympathetic nerves innervating the heart have dopamine receptors that serve an inhibitory role in transmission. 15 references. (Author abstract modified)

210890 Roubein, I. F.; Samuelly, M.; Keup, W. Saul R. Korey Department of Neurology, Albert Einstein College of Medicine, Bronx, NY 10461 **The toxicity of chlorpromazine and mescaline on mouse cerebellum and fibroblast cells in culture.** Acta Pharmacologica et Toxicologica (Kobenhavn). 33(5-6):326-329, 1973.

The toxicity of chlorpromazine (CPZ) and mescaline (MCL) to mouse cerebellum and fibroblast cells was studied in vitro. CPZ proved to be more toxic than MCL to both tissues. Fibroblast cells are more sensitive than the cerebellum to both CPZ and MCL. 9 references. (Author abstract)

210891 Alhava, Eeva. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Modification by L-DOPA methylester (H 19/61) of amphetamine-induced brain catecholamine changes, thermal responses and toxicity in developing mice.** Acta Pharmacologica et Toxicologica (Kobenhavn). 33(5-6):330-347, 1973.

The effect of L-DOPA methylester on brain catecholamines was studied in adult and developing mice aged 3-5 days and 13-15 days. Noradrenaline was moderately increased in the developing brain but dopamine showed a manyfold increase. The increase of dopamine was less pronounced in adult brain. High doses of dl-amphetamine injected to L-DOPA pretreated mice further increased the dopamine levels in the developing brain. The adult brain catecholamines were remarkably depleted. Amphetamine lowered the body temperature in mice aged 13-15 days; the fall was dose dependent and potentiated by pretreatment with L-DOPA. In adult mice amphetamine caused hyperthermia which was not modified by L-DOPA. L-DOPA did not change the mortality rates induced by amphetamine in developing mice, but infant mice pretreated with L-DOPA showed a lower brain amphetamine concentration after death than the mice given amphetamine only. In adult mice L-DOPA enhanced amphetamine toxicity. 28 references. (Author abstract modified)

210892 Nielsen, I. Moller, Pedersen, V.; Nymark, M.; Franck, K. F.; Boeck, V.; Fjalland, B.; Christensen, A. V. Department of Pharmacology and Toxicology, H. Lundbeck & Co. A/S, Ottiliavej 7-9, DK-2500, Copenhagen-Valby, Denmark **The comparative pharmacology of flupenthixol and some reference neuroleptics.** Acta Pharmacologica et Toxicologica (Kobenhavn). 33(5-6):353-362, 1973.

Flupenthixol, a thioxanthene derivative which exists in two isomeric forms, alpha and beta, was examined. Flupenthixol contains 45-55% alpha-flupenthixol. The pharmacological effects of flupenthixol, alpha and beta-flupenthixol were compared with those of clopenthixol, chlorprothixene, fluphenazine, perphenazine, chlorpromazine and haloperidol. In most pharmacological screening tests alpha-flupenthixol was equipotent with fluphenazine. Beta-flupenthixol showed very low pharmacological activity. The potency of flupenthixol was about one half that of alpha-flupenthixol. Flupenthixol was considerably more potent than clopenthixol and chlorprothixene in the inhibition of conditioned avoidance response. The influence on temperature regulation and the peripheral alpha-adrenolytic effect was considerably weaker than that of chlorprothixene. 11 references. (Author abstract)

210893 Nymark, M.; Franck, K. F.; Pedersen, V.; Boeck, V.; Nielsen, I. Moller. Department of Pharmacology and Toxicology, H. Lundbeck & Co. A/S, Ottiliavej 7-9, DK-2500, Copenhagen-Valby, Denmark **Prolonged neuroleptic effect of alpha-flupenthixol decanoate in oil.** Acta Pharmacologica et Toxicologica (Kobenhavn). 33(5-6):363-376, 1973.

The duration and intensity of the neuroleptic effect of alpha-flupenthixol decanoate in viscoleo were compared with that of alpha-flupenthixol, HCl in aqueous solution and alpha-flupenthixol base in viscoleo in a number of animal experimental models. Incorporation of alpha-flupenthixol base in oil led to a prolongation of the neuroleptic effect (apomorphine antagonism in dogs, inhibition of conditioned avoidance in rats and mice) as compared to the duration of the effect of alpha-flupenthixol, HCl in aqueous solution. In both cases marked sedation was observed. In contrast, there was no sedation after alpha-flupenthixol decanoate in oil, but a slower, smoother onset and a much longer duration of neuroleptic effect resulted. In rats the cataleptic effect and the apomorphine antagonistic effect of alpha-flupenthixol decanoate in oil were of much shorter duration than the inhibitory effect on condi-

tioned avoidance response. In mice a slight potentiation of barbiturate anesthesia could be demonstrated 1-6 hrs after high doses of alpha-flupenthixol decanoate in oil. The clinical advantages of the depot preparation are discussed. 4 references. (Author abstract)

210900 Gerald, Michael C.; Hsu, Song Y. Division of Pharmacology, College of Pharmacy, Ohio State University, Columbus, OH 43210 **Effects of methamphetamine on the isolated rat phrenic nerve-diaphram preparation.** Research Communications in Chemical Pathology and Pharmacology. 10(2):395-398, 1975.

The effects of methamphetamine on the isolated rat phrenic nerve diaphragmparation were examined. Low concentrations of methamphetamine facilitated twitch, while higher concentrations produced dose dependent blockade of twitch indirectly elicited. Methamphetamine facilitated twitch elicited by direct stimulation. These findings suggest that methamphetamine induced enhancement in physical endurance and performance in moderate doses, and muscle weakness at high doses, may be attributed to drug effects at a peripheral site of action. 9 references. (Author abstract)

210902 Goldberg, Leon I. Clinical Pharmacology Committee, University of Chicago, Chicago, IL 60637 **The dopamine vascular receptor.** Biochemical Pharmacology (Oxford). 24(6):651-653, 1975.

The dopamine vascular receptor was reviewed. Dopamine increases cardiac contractility and heartrate. These effects are due both to direct action on receptors and to release of norepinephrine from adrenergic nerve terminals in the myocardium. Dopamine induced contraction has been demonstrated in arteries and veins, and this phenomenon must be eliminated before relaxing effects can be quantitatively assessed. Such selective vasodilation certainly suggests the existence of a dopamine receptor. However, two problems have not yet been answered. First, the order of potency of a series of closely related analogs must be determined and found to be similar in all tissues whose responses are considered to be due to action on the receptor. Second, specific antagonism must be demonstrated. Selective antagonism of dopamine induced renal and mesenteric vasodilation has been demonstrated with haloperidol, and other butyrophenones, several phenothiazines, and bulbocapnine. Finally, precise quantitation of agonist and antagonist relationships requires an isolated organ system since other mechanisms could be involved in the vasodilation in the intact animal. 25 references.

210903 Maheshwari, Usha R.; Chan, Sin-Lam; Trevor, Anthony J. Department of Pharmacology, University of California, San Francisco, CA 94143 **Reversible inhibition of mammalian brain acetylcholinesterase and sodium potassium-stimulated adenosine triphosphatase by cyclopropane.** Biochemical Pharmacology (Oxford). 24(6):663-669, 1975.

Membrane bound and purified forms of acetylcholinesterase (AChE) derived from beef brain caudate nucleus tissue were inhibited reversibly by cyclopropane at low gas pressures. Inhibition followed mixed kinetics which suggested interactions of the anesthetic gas with both active sites(s) and other sites on the enzyme molecule. At gas pressures of 1 atm and higher, cyclopropane inhibited membrane bound and solubilized preparations of brain sodium - potassium (Na-K) ATPase without affecting magnesium ATPase activity. This inhibition was reversible, followed uncompetitive kinetics and was not due to pressure per se. AT32P labeling experiments suggested that cyclopropane inhibited Na-K-ATPase at or before the phosphorylation step in the enzyme reaction cycle. 29 references. (Author abstract)

210904 Hunt, Peter F.; Kannengiesser, Marie-Helene; Raynaud, Jean-Pierre. Centre de Recherches Roussel-Uclaf 93230 Romainville, France **The nature of (3H)imipramine binding to synaptosomes.** Biochemical Pharmacology (Oxford). 24(6):681-685, 1975.

In a study of imipramine binding to synaptosomes, it was found that in contrast to serotonin uptake, the saturable binding of imipramine to rat brain synaptosomes does not involve an active transport process, since it is independent of time, temperature and sodium, potassium - ATPase. It is unaffected by a high concentration of serotonin, confirming that the uptake site for this amine is not implicated. Diverse psychoactive compounds effectively compete with imipramine for binding to synaptosomal membranes and the order of their activity is correlated with their lipophilicity. It is suggested that these compounds interact with a lipophilic pocket of low affinity and low specificity. If a more specific interaction exists and is associated with inhibition of transmitter amine uptake by tricyclic antidepressants, it could be masked by this process. 18 references. (Author abstract modified)

210918 Hutchison, J. B. MRC Unit, University Sub-Department, Modingley, Cambridge, England **Post-castration decline in behavioural responsiveness to intrahypothalamic androgen in doves.** Brain Research (Amsterdam). 81(1):169-181, 1974.

Postcastration decline in behavioral responsiveness to intrahypothalamic androgen in doves is reported. Intramuscular treatments of testosterone propionate (TP) were less effective in evoking precopulatory aggressive and nest orientated behavior in long-term (90 day) than in short-term (15 day) castrated male doves. To determine whether this effect was due to a change in androgen sensitivity of hypothalamic and associated brain mechanisms underlying this behavior, crystalline implants of TP were positioned into the region of the nucleus preopticus medialis and nucleus hypothalamicus anterior medialis areas at 15, 30 and 90 days after castration. The behavioral effects were inversely related to the period between castration and implantation. Aggressive and nest orientated behavior were restored in most 15 day castrates but there were deficits in the aggressive behavior of 30 day castrates relative to precastration levels and TP into 90 day castrates was either ineffective or induced low levels of courtship behavior. The results indicate that hypothalamic and associated brain mechanisms underlying precopulatory behavior become less sensitive to exogenous androgen with time after castration. It is suggested that gonadal androgen participates in the maintenance of the hormone sensitivity of preoptic and anterior hypothalamic mechanisms associated with male precopulatory sexual behavior. 21 references. (Author abstract)

210919 Palkovits, M.; Richardson, J. S.; Jacobowitz, D. M. Department of Anatomy, Semmelweis University Medical School, 1450 Budapest, Tuzolto u. 58, Hungary **A histochemical study of ventral tegmental acetylcholinesterase-containing pathway following destructive lesions.** Brain Research (Amsterdam). 81(1):183-188, 1974.

The ventral tegmental acetylcholinesterase containing pathway was examined following destructive lesions. The data suggest that the ventral tegmental pathway originates from the cuneiform and dorsolateral tegmental nuclei. The fibers pass ipsilaterally along the lateral region of the mesencephalon to the lemniscus lateralis. More rostrally and ventrally, they reach the lateral aspect of the lemniscus medialis and ascend

in the medial direction. At the mammilary level, they concentrate the circumscribed VTP and possibly join with some other fibers. 12 references.

210921 Cheng, H. C.; Long, J. P.; Nichols, D. E.; Berfknecht, C. F.; Rusterholz, D. B. Department of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52242 **Effects of rigid amphetamine analogs on vascular strips: studies of 2-aminotetrahydronaphthalene and 2-aminoindan derivatives.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 208(2):264-273, 1974.

In order to investigate the mechanism by which 2-aminotetrahydronaphthalene (aminotetralin (AT)) and 2-aminoindan analogs influence sympathetically innervated vascular smooth muscle, effects of these rigid analogs were studied on superfused strips of dog dorsal metatarsal veins. The following compounds were tested: 2-AT, 5,8-diamethoxy-2-aminotetralin(5,8-ADT), 5,8-dimethoxy-6-methyl-2-aminotetralin (DOM-AT) and 4,7-dimethoxy-5-methyl-2-aminoindan (DOM-AI). Results demonstrate that AT stimulated adrenergic receptors indirectly by releasing norepinephrine from sympathetic nerve terminals whereas, 5,8-ADT activates alpha-adrenergic receptors directly. 5,8-ADT, DOM-AT and DOM-AI possess serotonin (5-HT) receptor stimulatory acitivty. The rigid analogs are much more potent than their corresponding amphetamine derivatives. Thus AT, 5,8-ADT and DOM-AT are more potent than d-amphetamine, 2,5-dimethoxyamphetamine and 2,5-dimethoxy-4-methylamphetamine respectively. 16 references. (Author abstract)

210922 Fuller, R. W.; Baker, J. C.; Perry, K. W.; Molloy, B. B. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Effect of phenobarbital on the metabolism and serotonin-depleting action of 4-chloro-beta,beta-difluoroamphetamine in rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 208(2):274-278, 1974.

The effect of phenobarbital on the metabolism of serotonin depleting action of 4-chloro-beta,beta-difluoroamphetamine was examined in rats. Pretreatment of rats with phenobarbital to induce hepatic microsomal enzymes markedly accelerated the disappearance rate of 4-chloro-beta,beta-difluoroamphetamine from brain, liver, and dpididymal fat in rats, without affecting the disappearance rate of 4-chloroamphetamine. Because of the increased rate of metabolic destruction of 4-chloro-beta,beta-difluoroamphetamine, the ability of that drug to deplete brain 5-hydroxyindoles was prevented by phenobarbital pretreatment. These data suggest that 4-chloro-beta,beta-difluoroamphetamine acts directly rather than through a metabolite on brain 5-hydroxyindoles. 7 references. (Author abstract)

210923 Cowan, A.; Ghezzi, D.; Samanin, R. Department of Pharmacology, Reckitt and Colman, Hull, England **Effect of midbrain raphe lesion and of 6-hydroxydopamine on the antinociceptive action of buprenorphine in rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 208(2):302-305, 1974.

The role of brain monoamines in the central mediation of the antinociceptive effect of buprenorphine was investigated in rats using the tail compression test. The antinociceptive action of buprenorphine was not significantly influenced in rats injected intraventricularly with 6-hydroxydopamine or lesioned in the midbrain raphe. These findings suggest that lowered concentrations of dopamine and noradrenaline or 5-hydroxytryptamine have little effect on the activity of buprenorphine in this pain situation. 14 references. (Author abstract)

210925 Guerrero, S.; Molgo, J. Department of Pharmacology, University of Chile, P.O. Box 16387, Santiago 9, Chile **Effects of imipramine upon frog nerve excitability and conduction.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 209(1):26-37, 1974.

The effects imipramine on frog nerve excitability and conduction were examined. Imipramine inhibits excitability and blocks impulse conduction of desheathed from sciatic nerves. Imipramine, as well as lidocaine, depresses and distorts the nerve excitability recovery curve. A lengthening of the relative refractory period and a slowing of the conduciton velocity of the nerve is also observed during blockade with imipramine. The method employed, however, does not allow to measure drug effects on individual axons. The intensity of action upon time constant, action potential amplitude, relative refractory period and conduction velocity obtained at pH 6.5are compared with those at pH 8.5. Imipramine appears in this respect about one third less active at pH 8.5than at pH 6.5. The mechanism of action of imipramine seems to be similar to that accepted for local anesthetics. 16 references. (Author abstract)

210926 Glick, S. D.; Marsanico, R. G. Department of Pharmacology, Mount Sinai School of Medicine, 5th Ave. and 100th St., New York, NY 10029 **Comparative time-dependent changes in sensitivity to locomotor effects of d-amphetamine in mice with caudate, hippocampal or frontal cortical lesions.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 209(1):80-85, 1974.

In a study of time dependent changes in the sensitivity to locomotor effects, different groups of mice with bilateral lesions of either the caudate, hippocampus or frontal cortex were tested once in activity cages following a dose of d-amphetamine or saline at either 1 day or 1 month after surgery. Mice with caudate lesions were less sensitive to d-amphetamine at 1 day after surgery. At 1 month after surgery, d-amphetamine sensitivity in mice with caudate lesions was normal. Sensitivity to d-amphetamine in mice with hippocampal or frontal lesions was normal at 1 day after surgery but was enhanced at 1 month after surgery; with both lesions, such increased sensitivity occurred to a greater extent with lower doses of d-amphetamine. These results suggested that the caudate may mediate all locomotor effects of d-amphetamine but that different synaptic actions of d-amphetamine within the caudate may be related to the different kinds of motor behaviors elicited by low and high doses of d-amphetamine. Time dependent changes in d-amphetamine sensitivity following all three lesions were consistent with denervation supersensitivity. 17 references. (Author abstract)

210927 Roffman, Mark; Reigle, Thomas; Orsulak, Paul; Schildkraut, Joseph J. Neuropsyhcopharmacology Laboratory, Massachusetts Mental Health Center, Boston, MA 02115 **The effects of acute and chronic morphine administration on the levels of 3-methoxy-4-hydroxyphenylglycol sulfate in rat brain.** Research Communications in Chemical Pathology and Pharmacology. 10(3):403-417, 1975.

The acute and chronic effects of morphine on the turnover of norepinephrine (NE) were determined by measuring the changes in the levels of the sulfate conjugate of 3-methoxy-4-hydroxyphenylglycol (MHPG-SO4) in rat brain. Two hours after administration, morphine produced a dose related increase in the levels of MHPG-SO4 suggesting an increase in NE turnover. The effect of morphine was evident by 1 hour after drug administration and was maintained for at least 4 hours but disappeared by 8 hours. Chronic treatment with morphine resulted in lower baseline levels of MHPG-SO4 and

the development of tolerance to its acute effect on NE turnover. These findings suggest that after chronic administration of morphine, the maintenance of a normal rate of norepinephrine turnover in brain is dependent upon the continued administration of maintenance doses of morphine. 26 references. (Author abstract)

210928 Kumbar, Mahadevappa; Sankar, D. V. Siva. Division of Research Laboratories, Queens Children's Psychiatric Center, Bellerose, NY 11426 **Preferred conformations of serotonin in relation to receptor sites.** Research Communications in Chemical Pathology and Pharmacology. 10(3):433-442, 1975.

Using an empirical method, three preferred conformations for serotonin have been predicted. These three conformations correspond to one extended form and two folded forms. The calculated intramolecular distances in both forms agree with those obtained by the X-ray cyrstallography of various indoleamines. The dual receptor binding activity of serotonin is explained in terms of extended and folded conformations. 11 references. (Author abstract)

210929 Parli, C. John; Schmidt, Barbara. Lilly Research Laboratories, Indianapolis, IN 46206 **Metabolism of 4-chloroamphetamine to 3-chloro-4-hydroxyamphetamine in rat: evidence for an in vivo "NIH shift" of choline.** Research Communications in Chemical Pathology and Pharmacology. 10(3):601-604, 1975.

The metabolism of 4-chloroamphetamine (PCA) to 3-chloro-4-hydroxyamphetamine in the rat was studied. It was found that the 3-chloro-4-hydroxyamphetamine metabolite was an in vivo metabolite of PCA in the rat. It is suggested that the excreted metabolite was probably formed in the liver via an NIH shift of the choline atom. The proposed bioactivated intermediate in the NIH shift is thought to be an arene oxide, a highly reactive species which could cause cell damage or destruction by reaction with cellular components. 12 references.

210932 Phillis, John W.; Kostopoulos, George K.; Limacher, James J. Department of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Canada **A potent depressant action of adenine derivatives on cerebral cortical neurones.** European Journal of Pharmacology (Amsterdam). 30(1):125-129, 1975.

A potent depressant action of adenine derivatives on cerebral cortical neurons is presented. Adenosine and several adenine nucleotides depress the excitability of cerebral cortical neurons, including identified Betz cells. Cyclic 3',5'-adenosine monophosphate was a less effective depressant than various other adenine nucleotides, including cyclic 2',3'-adenosine monophosphate. Adenine and inosine had only weak depessant activity. An initial excitant action of ATP was observed on several neurons. This was succeeded by a depressant effect when the application of ATP was terminated. 11 references. (Author abstract)

210933 Anderson, Thomas R.; Schanberg, Saul M. Laboratory of Neuropharmacology, Center for Cerebrovascular Research, Durham, NC **Effect of thyroxine and cortisol on brain ornithine decarboxylase activity and swimming behavior in developing rat.** Biochemical Pharmacology (Oxford). 24(4):495-501, 1975.

Thyroxine and cortisol were tested to determine their effects on the ontogenetic pattern of ornithine decarboxylase (ODC) activity in rat brain. The effects of both hormones were significant but varied with the brain region studied and with the age of the rat. Thyroxine altered ODC activity in all brain regions studied, if given during the first 10 postnatal days. The magnitude of the response to thyroxine was greater in the cerebellum, followed by the cerebrum and brainstem respectively. Cortisol, when given on the first postnatal day initially depressed ODC activity and subsequently prolonged the time required to reach the low level of activity found normally in adult brain. The data are consistent with the hypothesis that thyroxine and cortisol, when administered to the neonate, may exert some of their effects on nucleic acid metabolism and ultimately growth, development and behavior via their effects on polyamine metabolism. 29 references. (Author abstract modified)

210973 Christensen, J. Dencker. Department of Pharmacology, Royal Danish School of Pharmacy, 2 Universitetsparken, DK-2100 Copenhagen, Denmark **Tolerance development with chlordiazepoxide in relation to the plasma levels of the parent compound and its main metabolites in mice.** Acta Pharmacologica et Toxicologica (Kobenhavn). 33(4):262-272, 1973.

Tolerance development with chlordiazepoxide in relation to the plasma levels of the parent compound and its main metabolites in mice was examined. A single pretreatment with chlordiazepoxide, HCl to male mice produced tolerance to the compound 24 hours later as measured by the performance on a modified rotarod (the rotacone). The plasma levels of chlordiazepoxide and the major metabolites 7-chloro-2-amino-5-phenyl-3H,1,4-benzodiazepine-4-oxide (D-M) and 7-chloro-1,3-dihydro-5-phenyl-2H-1,4-benzodiazepine-2-one-4-oxide (lactam) were determined in mice acutely and repeatedly treated with chlordiazepoxide. Although a single pretreatment of chlordiazepoxide HCl increases the rate of metabolism, other factors must be involved to explain the tolerance developed. Mice treated twice with chlordiazepoxide 165mg/kg had significantly higher plasma levels of the compound and its metabolites 10 and 30 minutes after the second injection as compared with mice receiving 50mg/kg chlordiazepoxide, HCl acutely, while the performance on the rotacone was similar in the two groups. Chlordiazepoxide had the most potent effect in the rotacone test, D-M and lactam were about equipotent. 6 references. (Author abstract)

211009 Levy, R. H.; Lockard, J. S.; Green, J. R.; Friel, P.; Martis, L. Department of Pharmaceutical Sciences, School of Pharmacy, University of Washington, Seattle, WA 98195 **Pharmacokinetics of carbamazepine in monkeys following intravenous and oral administration.** Journal of Pharmaceutical Sciences. 64(2):302-307, 1975.

The pharmacokinetics of carbamazepine were evaluated in four male rhesus monkeys. A 20mg/kg dose was administered by intravenous infusion and orally in a propylene glycol - ethanol - water solvent. Plasma and urine determinations were performed by gas - liquid chromatography. All semilogarithmic intravenous curves exhibited an irregular decay behavior in the first 3 hr period, followed by a linear disappearance phase. Urinary excretion measurements confirmed the short elimination half-life and showed that less than 1% of the dose was excreted unchanged. Oral studies also yielded a short elimination half-life which was confirmed by urinary excretion measurements. The oral curves were analyzed pharmacokinetically. The fraction of the dose reaching the systemic circulation ranged between 58 and 87%. Measurable amounts of drug were found in the feces after intravenous and oral administrations. 21 references. (Author abstract modified)

211062 Storm-Mathisen, Jon. Norwegian Defense Research Establishment, Division for Toxicology, N-2007 Kjeller, Norway **High affinity uptake of GABA in presumed GABA-ERGIC nerve endings in rat brain.** Brain Research (Amsterdam). 84(3):409-427, 1975.

High affinity uptake of gamma-aminobutyric acid (GABA) in presumed GABAergic nerve endings in rat brain was examined. After interruption of the striato - nigral pathway uptake of GABA in the substnatia nigra decreased within 7 days to a constant level 30-40% of the normal. Concomitantly glutamate decarboxylase (GAD) was reduced to 10%. Hence about 66% of the GABA uptake activity in substantia nigra are localized to the alleged GABAergic nerve elements originating from corpus striatum. Whereas GAD was recovered mainly in a heavy nerve ending fraction, a large proportion of the GABA uptake was situated in a light fraction. After hemisections, GABA uptake was reduced to a similar extent in both fractions. It is suggested that whereas GAD is concentrated in nerve terminals, a significant proportion of the GABA uptake may be localized in preterminal axon branches in the substantia nigra. GABA uptake in the dorsal part of the lateral vestibular nucleus was not reduced by interruption of the Purkinje axons fro the cerebellar vermis whereas GAD was reduced by 50%. This indicates that the reuptake mechanism is not concentrated in the Purkinje axon terminals. The order of ratios of GABA uptake to particulate GAD activity in different regions was: hippocampus; cerebellar cortex; substantia nigra; dorsal part of lateral vestibular nucleus; and nucleus interpositus. 54 references.

211063 Rebec, George V.; Groves, Philip M. Department of Psychology, University of Colorado, Boulder, CO 80302 **Differential effects of the optical isomers of amphetamine on neuronal activity in the reticular formation and caudate nucleus of the rat.** Brain Research (Amsterdam). 83(2):301-318, 1975.

The activity of neurons in the caudate nucleus and reticular formation was recorded following intraperitoneal injection of the optical isomers of amphetamine. D-amphetamine sulfate produced an initial increase in firing rate of neurons in the caudate nucleus approximately 8-10 min following intraperitoneal injection, and a subsequent depression of firing rate which lasted for a period of time of from 70 to 120 min. Similar injections of L-amphetamine sulfate produced only a depression of activity in the caudate nucleus which was less marked and of lesser duration. Mephentermine sulfate, a peripheral sympathomimetic, did not produce these effects. Both D-amphetamine and L-amphetamine sulfate at the same dose produced an increase in firing rate of neurons in the reticular formation, although that produced by the L-isomer was less marked and of lesser duration. In the caudate nucleus, a rebound increase in firing rate was observed following the marked depression produced by both isomers of amphetamine. A rebound depression of activity was observed in the reticular formation following the initial increase in neuronal activity produced by these drugs. 45 references.

211065 Saelens, J. K.; Simke, J. P.; Schuman, J.; Allen, M. P. Pharmaceuticals Division, Ciba-Geigy Corporation, Summit, NJ 07901 **Studies with agents which influence acetylcholine metabolism in mouse brain.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 209(2):250-258, 1974.

By using an intravenous single pulse injection of choline-C14 into the tail vein of mice and measuring the endogenous levels of choline and acetylcholine, the effects of agents which influence acetylcholine metabolism in mouse brain were studied. The results were consistent with a feedback activation of cholinergic neurons with scopolamine, choline-0-acetyltransferase inhibition with naphthylvinylpyridine, inhibition of acetylcholine release by morphine and cholinesterase inhibition with physostigmine. The interactions of these agents with the cholinergic system further suggests certain characteristics of cholinergic neurons, e.g. that choline-0-acetyltransferase activity is accelerated by a decrease in intracellular acetylcholine levels and retarded by an increase in intracellular acetylcholine levels, that the choline transport mechanism is functioning at maximum capacity under normal physiological conditions and that the synaptic levels of endogenous choline play a role in tracer choline capture. 12 references. (Author abstract modified)

211066 De Moraes, S. Laboratory of Therapeutics, Faculty of Veterinary Medicine, University of Sao Paulo, Sao Paulo, Brazil **The effects of (+)-amphetamine on the chronotropic responses of the isolated guinea-pig pacemaker to norepinephrine and isoproterenol.** Archives Internatinales de Pharmacodynamie et de Therapie (Ghenr). 210(2):256-267, 1974.

The effects of (+)-amphetamine on the chronotropic responses of the isolated guinea-pig pacemaker to norepinephrine (NE) tryamine and isoproternol were examined. After pretreatment of guinea pigs with reserpine 24 hr prior to the experiments or with a combination of reserpine alpha-methyltyrosine 4-6hr before sacrifice the spontaneous rate of contractions of the isolated guinea pig pacemaker was not affected, suggesting that the resting rate of the preparation is independent of the endogenous levels of norepinephrine (NE). The positive chronotropic effect of (+)-amphetamine was reduced following pretreatment with reserpine and prevented by the schedule of pretreatment with reserpine and alpha-methyltyrosine. An estimation of the NE releasing effect of the drug was performed. Consistent with the results obtained with the chronotropic effects of the sympathomimetic amine the NE releasing effect was reduced by reserpine and abolished with reserpine and alpha-methyl-tyrosine. It is suggested that the indirect sympathomimetic effects of (+)-amphetamine in peripheral tissues can be partially linked to a release of newly synthetized neurotransmitter in a mode of action similar to that described for the central stimulant effects of the drug. 34 references. (Author abstract modified)

211099 Laurent, B.; Roy, P. E; Gailis, L. Centre de recherche, Institut de cardiologie de Quebec, 2725, chemin Ste-Foy, Quebec G1V 4G5, Canada **Inhibition of delta1-tetrahydrocannabinol of Na+-K+ transport ATPase from rat ileum. Preliminary report.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(6):1110-1113, 1974.

The effect of delta1-trans-tetrahydrocannabinol (THC) on ATPase activities of a microsomal fraction from rat ileum was measured. THC abolished the stimulation due to sodium and potassium, whereas the activity of the magnesium - ATPase was about 60% of the control. Even at concentrations found in blood after smoking one marihuana cigarette there was a slight inhibition of the sodium - potassium - ATPase. The inhibition may be due to a specific binding or, more likely, to a general action of the THC on membranes. 20 references. (Author abstract)

211100 Siemens, A. J.; Kalant, H. Research Institute on Alcoholism, 1021 Main Street, Buffalo, NY 14203 **Metabolism of delta1-tetrahydrocannabinol by rats tolerant to cannabis.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(6):1154-1166, 1974.

The metabolism of delta1-tetrahydrocannabinol (THC) by rats tolerant to cannabis was examined. Daily treatment of rats with phenobarbital for 5 days resulted in an induction of the metabolism of THC in vitro and in vivo. Although the Km and Vmax for THC metabolism by liver preparations in vitro were not altered, the rate of formation of highly polar THC metabolites was significantly increased. Phenobarbital also significantly increased the rate of biliary excretion of THC and its metabolites and their disappearance from the blood and tissues. Rats were shown to become tolerant on chronic treatment with marihuana extract, as indicated by a reduction in marihuana induced enhancement of ethanol sleeping time. The biliary excretion, disappearance from the blood, and residual tissue levels of THC and its metabolites were not altered in the tolerant animals compared to pair fed and ad libitum fed controls. 33 references. (Author abstract modified)

211101 Jaramillo, J.; Greenberg, R. Department of Pharmacology, Ayerst Research Laboratories, Montreal, Quebec H3C 3J1 **Comparative pharmacological studies on butriptyline and some related standard tricyclic antidepressants.** Canadian Journal of Physiology and Pharmacology (Ottawa). 53(1):104-112, 1975.

Butriptyline was compared with imipramine and other tricyclic antidepressants for its ability to modify contractions of the cat nictitating membrane induced by noradrenaline (NA) and 5-hydroxytryptamine (5-HT), the adrenergic neuron blocking action of guanethidine in the guinea-pig vas deferens, the rabbit's electroencephalogram (EEG) and physostigmine arousal, and the sleep pattern of the rat. Imipramine and amitriptyline potentiated the NA and 5-HT effects on the nictitating membrane and antagonized the inhibitory actions of guanethidine in the guinea-pig vas deferens, whereas iprindole and butriptyline were ineffective. These results are consistent with the ability of these drugs to block the neuronal uptake of catecholamines. Butriptyline was a potent blocker of the arousal reaction induced by physostigmine. Butriptyline and amitriptyline reduced rapid eye movement sleep with a concomitant increase in nonrapid eye movement sleep. This may be a reflection of the dual activity observed in the clinic with these compounds, namely, antidepressant and antianxiety effects. 39 references. (Author abstract)

211102 Bourdois, P. S.; McCandless, D. L.; MacIntosh, F. C. 6 rue du Carroi du Gaufre, 37150 Blere, France **A prolonged after-effect of intense synaptic activity on acetylcholine in a sympathetic ganglion.** Canadian Journal of Physiology and Pharmacology (Ottawa). 53(1):155-165, 1975.

A prolonged aftereffect of intense synaptic activity on acetylcholine in a sympathetic ganglion was reported. The finding was confirmed that there is a rebound increase of stored acetylcholine (ACh) in cat superior cervical ganglia conditioned by prolonged preganglionic stimulation at a frequency high enough to cause initial depletion of the store. The appearance of rebound ACh during and after conditioning stimulation was suppressed by hexamethonium and by tubocurarine, neither of which has much effect on ACh turnover in ganglia excited at lower frequencies, but not by atropine, noradrenaline, or phenoxybenzamine. The formation of rebound ACh is thus contingent on the postsynaptic nicotinic response to released ACh, and may represent an augmentation of the transmitter store in structures remote from the release sites. 38 references. (Author abstract modified)

211104 Fuller, Ray W.; Snoddy, Harold D.; Molloy, Bryan B. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Potentiation of the L-5-hydroxytryptophan-induced elevation of plasma corticosterone levels in rats by a specific inhibitor of serotonin uptake.** Research Communications in Chemical Pathology and Pharmacology. 10(1):193-196, 1975.

The ability of L-5-hydroxytryptophan (L-5HTP), a serotonin precursor, to elevate plasma levels of corticosterone in rats was confirmed. Pretreatment of the rats with 3-(p-trifluoromethylphenoxy)-N-methyl-3-phenyl-propylamine hydrochloride (Lilly 110140) markedly enhanced the elevation of corticosterone levels by L-5HTP. Since Lilly 110140 is a specific inhibitor of serotonin uptake, these results support the hypothesis that L-5HTP elevates corticosterone by enhancing neurotransmission through a serotoninergic pathway influencing adrenocorticotropic hormone release. 6 references. (Author abstract)

211106 Mrsulja, B. B.; Rosic, N. Laboratory for Neurochemistry, Institute of Biochemistry, Faculty of Medicine, YU-11000 Belgrade, Yugoslavia **The effect of reserpine and chlorimipramine on glycogen content in different brain structures of rat.** Experientia (Basel). 30(12):1434-1435, 1974.

In a study of the effect of reserpine and chlorimipramine on glycogen content in the rat brain, reserpine was found to markedly increase glycogen content in all brain structures of treated animals to a significant degree. The most pronounced effects of reserpine were found after 26 and 28 hours. Chlorimipramine exerted biphasic action on glycogen concentration in rat brain. Two hours after administration, glycogen content was significantly decreased in all tested structures of brain; but 6 hours after administration glycogen content was markedly increased over control values in all structures except the thalamus. Chlorimipramine decreased glycogen concentration in reserpine treated animals, but only if it was measured 2 hours after chlorimipramine injection (or 24 hours after reserpine.)Six hours after chlorimipramine treatment, glycogen content was found to have increased. 15 references.

211111 Lal, S.; Sourkes, T. L.; Missala, K. Department of Psychiatry and Biochemistry, McGill University, Montreal, Quebec, Canada **The effect of certain tranquilisers, chlorpromazine metabolites and diethyldithiocarbamate on tissue amphetamine levels in the rat.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 207(1):122-130, 1974.

The effects of chlordiazepoxide, diazepam and diethyldithiocarbamate on amphetamine induced stereotyped behavior (ASB) and tissue amphetamine levels were examined. In the case of diazepam pretreated rats, tissue amphetamine levels were elevated 2 hr after amphetamine administration but by 4 hr there was no difference from rats receiving amphetamine alone. Chlorpromazine, chlorpromazine-N-oxide and chlorpromazine sulfoxide increased the half-life of amphetamine in brain. It is suggested that chlorpromazine metabolites contribute to the effect of the parent compound on amphetamine metabolism. Perphenazine, trifluoperazine and thioproperazine also increased the half-life of amphetamine in brain but, despite this increase, ASB was completely inhibited. 33 references. (Author abstract)

211112 Siemens, Albert J.; Kalant, Harold. Research Institute on Alcoholism, 1021 Main St., Buffalo, NY 14203 **Metabolism of delta1-tetrahydrocannabinol by the rat in vivo and in vitro.** Biochemical Pharmacology (Oxford). 24(7):755-762, 1975.

The metabolism of (14C)delta1-tetrahydrocannabinol (THC) was examined in vitro employing the supernatant (10KS) of rat liver homogenates, after determination of apparent optimal conditions. The extent of metabolism was greater when THC was added as a suspension in rat serum than in a glycol or ethanol solution. Thin layer chromatography indicated that at least seven metabolites were produced from THC, with the quantitative pattern of the metabolites changing dramatically with increasing duration of incubation. The metabolism of THC, rather than the excretory process, was apparently the rate limiting step in the elimination of the drug in the bile. When the biliary excretory mechanism was saturated, increase in the dose of THC resulted in increased urinary excretion of highly polar metabolites, but relative concentrations in tissues other than liver were unaffected. 36 references. (Author abstract modified)

211412 Schless, Arthur P.; Frazer, Alan; Mendels, Joe; Pandey, Ghanshyam N.; Theodorides, Vassilios J. Veterans Administration Hospital, University and Woodland Ave., Philadelphia, PA 19104 **Genetic determinant of lithium ion metabolism: II. An in vivo study of lithium ion distribution across erythrocyte membranes.** Archives of General Psychiatry. 32(3):337-340, 1975.

Two groups of sheep with genetically determined differences in their cation concentrations were administered lithium chloride for 10 days, to determine if membrane factors, known to influence the distribution of sodium ion (Na) and potassium ion (K), also influence lithium ion distribution. The low red blood cell (RBC) potassium ion sheep had a greater RBC lithium ion concentration than the high RBC potassium ion sheep. In vitro incubation of erythrocytes with lithium chloride also produced substantially different RBC lithium ion to plasma lithium ion ratios similar to those seen in the in vivo study. Distribution of lithium ion was generally similar to that of Na ion. It seems that lithium ion distribution may be controlled by the same genetic factors that regulate Na ion distribution. 21 references. (Author abstract)

211746 Khalsa, Jagjitsingh H. University of Mississippi **Behavioral and neurochemical effects of morphine or amphetamine after chronic pretreatment with catecholamine-depleting agents. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, ich., Univ. M-films, No. 75-519 HC$13.50 MF$5.00 131 p.

Morphine and amphetamine induced behavioral effects in rats were recorded. Hyperactivity induced by both morphine and amphetamine was significantly antagonized by the catecholamine depleting agents L-alpha-methyl-p-tyrosine (AMT) or U-14,624. Chronic treatment with AMT produced tolerance to its catecholamine depleting effects within 12 to 18 days. The significant reduction of feeding in rats suggested a possible involvement of central noradrenergic systems in the behavior. (Journal abstract modified)

212182 Lamarre, Y.; Dumont, M.; Joffroy, A. J. Centre de Recherehe en Sciences Neurologiques, Departement de Physiologie, Universite de Montreal, Quebec **/Parkinsonian type tremor and the action of harmaline: experimental facts and hypothetical mechanisms./** Le tremblement de type parkinsonien et l'action de l'harmaline: faits experimentaux et mecanismes hypothetiques. Archives Italiennes de Biologie (Pisa). 3(3-4):493-503, 1973.

The results of two experiments on monkeys were analyzed to derive a hypothesis of the origins and transmission of Parkinsonian type tremor. The first experiment tested the thalamocortical mechanism and results suggest that rhythmic activity in the ventrolateral thalamic region and the precentral cortex caused experimental Parkinsonian tremor. The second experiment related olivocerebellar rhythmicity to the central action of harmaline. The two groups of monkeys who formed the experimental population had had total and partial cerebellectomies. Results suggest that rhythmic olivocerebellar activity was generally in phase with periods of rapid tremor and that harmaline exaggerated the activity of the cells of the monkeys' thalamic pacemakers. The existence of a dual system in the monkey which could cause Parkinsonian tremor was hypothesized. An analytical and diagrammatical simplification of this combined system is presented. 28 references.

212520 Koller, William Carl. Northwestern University **Evoked neural activity in the basal ganglia of the cat and its modification by cholinergic and dopaminergic agents. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-28665 HC$13.50 MF$5.00 140 p.

The interrelationships between various structures making up the basal ganglia of the cat were defined in electrophysiological terms and the possibility of cholinergic and/or dopaminergic mechanisms being involved in these neuronal systems was determined. Evoked responses were recorded along previously well documented pathways, and a pallidonigral pathway was demonstrated, although nigro-pallidal responses were not seen. A direct connection was also suggested between the anterior caudates of the opposite hemispheres and the concept of a homogeneous neural organization within the caudate nucleus is supported. The data also support the concept that acetylcholine has a functional role in the basal ganglia. Cholinergic drugs had no effect on either caudate afferent or efferent responses, nor on any other basal ganglia evoked potentials. Data implicate the caudate interneuron as the site of caudate cholinergic activity. The effects of reserpine and L-dopa on basal ganglia evoked potentials were also investigated. (Journal abstract modified)

212521 Laird, Hugh Edward, II. University of Arizona **5-Hydroxytryptamine as an inhibitory modulator in audiogenic seizure. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-28294 HC$13.50 MF$5.00 100 p.

Evidence is presented which suggests that 5-hydroxytryptamine (5-HT) functions as an inhibitory modulator in the audiogenic seizure process in rats, and the brain regions in which 5-HT exerts this effect were determined. A circadian study shows that audiogenic seizure is enhanced during the dark period, the time when 5-HT in the brain is at lowest levels. Overall findings suggest that this compound and/or norepinephrine may serve as inhibitory modulators in seizure activity. Selective depletion of 5-HT was performed with p-chloromethamphetamine and p-chlorophenylalanine. During the early phase the potent anticonvulsant effect of the first compound masked the seizure enhancing effect of 5-HT depletion. During the late phase, after the anticonvulsant effect had subsided, the seizure enhancing effect of 5-HT depletion became more apparent. The time course study with p-chlorophenylalanine showed persistent enhancement of audiogenic seizure for 9 days. Results of other experimentation indicate that the biogenic amines, norepinephrine and 5-HT, are not involved in inhibiting the audiogenic seizure foci. (Journal abstract modified)

212522 Myslinski, Norbert Raymond. University of Illinois at the Medical Center **The role of 5-hydroxytryptamine in the con-**

trol of alpha and gamma motoneurons. (Ph.D. dissertation). Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-27298 HC$13.50 MF$5.00 120 p.

The role of 5-hydroxytryptamine (5-HT) in the control of alpha and gamma motoneurons was examined by facilitating and depressing the bulbospinal serotonergic system using both pharmacological and electrical methods. The resulting changes in the discharge rate of alpha and gamma motoneurons in lumbosacral ventral root filaments were also studied. In spinal deafferented cats the 5-HT precursors, l-tryptophan (TRY) and 5-hydroxytryptophan, and the monoamine oxidase inhibitor pargyline initiated spontaneous alpha activity and increased spontaneous gamma activity. Increases were the same in both extensor (gastrocnemius, and flexor (semitendinosus) motoneurons. This effect was potentiated by the 5-HT reuptake blocker imipramine and depressed by pretreatment with the TRY hydroxylase inhibitor, p-chlorophenylalanine. In decerebrate cats, stimulation of the n. raphe magnus evoked both alpha and gamma motoneurons at a latency that was compatible with the expected slow conduction velocity of 5-HT containing fibers. The 5-HT antagonists, cinanserin and methysergide blocked both pharmacologically and electrically evoked spikes. The serotonergic bulbospinal pathway descends to facilitate both alpha and gamma motoneurons. (Journal abstract modified)

212524 Thomson, Thomas Donald. University of Utah **Inhibition of sacral parasympathetic preganglionic neurons by GABA, glycine, 5-hydroxytryptamine and norepinephrine. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-25998 HC$13.50 MF$5.00 82 p.

Sacral parasympathetic preganglionic discharges recorded from the pelvic nerve were evoked by stimulation of sacral afferent fibers, descending pathways in the dorsolateral spinal cord or medullary vesicoconstrictor centers. Evoked activity was summed and integrated with a signal averaging computer in 67 spinal or decerebrate cats. Coadministration of picrotoxin and strychnine, but neither alone, increased evoked activity 4-10 times. After treatment with both drugs, the increases in bladder pressures evoked by stimulus trains were enhanced by 2-12 times. Bicuculline could be substituted for pictrotoxin. Similar increases in evoked pelvic nerve activity were induced by strychnine in cats depleted of gamma-aminobuturic acid (GABA) stores with semicarbazide. Overall results indicate that sacral parasympathetic preganglionic neurons are under strong, local tonic inhibition mediated by both GABA and glycine. The 5-hydroxytryptamine (5-HT) and norepinephrine bulbospinal neurons that terminate in the intermediolateral portion of the sacral spinal cord also appears to exert an inhibitory influence. Results are compatible with clinical experience in patients with loss of bladder function due to lesions of the spinal cord. (Journal abstract modified)

212547 Pass, Harold Lee. Boston University Graduate School **The effect of chlorpromazine and stimulation of the mesencephalic reticular formation on central arousal and on the visual evoked response. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-26463 HC$13.50 MF$5.00 118 p.

The effect of chlorpromazine (CPZ) and stimulation of the mesencephalic reticular formation (MRF) on central arousal and on the visual evoked response (VER) in rats was examined to gather relevant information for a current hypothesis regarding the causes for observed overarousal in schizophrenia. Stimulation of the MRF caused an increase in the percent of beta activity in the background electroencephalogram (EEG); CPZ caused a decrease in the percent beta in the background EEG. The antagonism, as demonstrated by the EEG data, indicates that CPZ acts on the MRF to reduce the level of cortical activation elicited by MRF stimulation. Evoked response data were difficult to interpret, as the increase in the amplitude of the VER elicited by stimulation appeared to be a poststimulation rebound phenomenon. Findings not only support the animal model of overarousal of Kornetsky and Eliasson, but also provide another significant link, via EEG, between the animal model and observed schizophrenic overarousal. (Journal abstract modified)

213050 Healy, Joan M. St. John's University **Psychomimetic substances during pregnancy and sex of offspring mice. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-3252 HC$13.50 MF$5.00 249 p.

The effects of the presence of psychotomimetic substances and symptoms of schizophrenia during pregnancy on the sex of the offspring were examined in mice in an attempt to replicate findings with human beings. It is assumed that a relationship exists which links autoimmune responses and failure of fibrinoid homeostasis to schizophrenia, pregnancy complications, psychotic symptoms following LSD ingestion, and silent abortion of males in early pregnancy. Following a review of the literature, mice were injected subcutaneously on the fifth day of pregnancy with saline, normal leukocytes, normal plasma, schizophrenic leukocytes, schizophrenic plasma, or LSD. A total lack of statistical significance of the data seemed to indicate that the absolute nature of the human findings, which suggest that no males are born of conceptions which take place within one month of onset of acute schizophrenic symptoms in the mother, and only females are born when LSD is taken during the first month of pregnancy, may be specific to humans. Suggestions for future research include use of other experimental animals, as well as different dosages, timing, and combinations of psychotomimetic substances. Studies of schizophrenia in humans might yield more consistent results if conducted during the first month following onset of symptoms. (Journal abstract modified)

213128 Dalhouse, Allan Derick. Ohio State University **The role of serotonin in the septal behavior syndrome of rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-3043 HC$13.50 MF$5.00 34 p.

Normal rats were injected with p-CPA, methysergide or control solutions to assess whether changes in serotonin mediate changes in emotionality and social cohesivness which follow lesions in the forebrain septum. Although p-CPA, which depletes serotonin, induced the Jonason-Enole effect, blockade of serotonin receptors with methysergide did not, nor did injections of 5-hydroxytryptophan, a serotonin repletor, reverse the enhancement of cohesivness as seen in rats prepared with lesions of the septum. Together, results suggest that the effects of p-CPA were not due to changes in levels of central serotonin, but, rather, to the somewhat less dramatic depletions of norepinephrine which were also brought about by systematic treatments with that compound. (Journal abstract modified)

213277 Weinrich, Daniel; Hammershlag, Richard. Department of Cell Biology and Pharmacology, University of Maryland School of Medicine, Baltimore, MD 21201 **Nerve impulse-enhanced release of amino acids from non-synaptic regions of peripheral and central nerve trunks of bullfrog.** Brain Research (Amsterdam). 84(1):137-142, 1975.

Isolated dorsal and ventral spinal roots of bullfrog were chosen to further characterize amino acid efflux from nerve trunks during impulse conduction, and to compare parameters of this release with those established for the release of substances from synaptic regions. Results indicate that depolarization per se is not a stimulus for enhanced amino acid release since exposing roots to increased concentrations of extracellular potassium (K+) over a 50 fold range had no major effect on the rate of efflux. Impulse enhanced efflux of amino acids may be linked to a particular event(s) associated with the generation of action potentials that must occur repetitively to lead to a detectable level of 14C material in the effluent. Such a process would not be simulated by K+ which acts to maintain the membrane in a depolarized state. Amino acid release from conducting axons thus differs from neurotransmitter release at nerve terminals which can be initiated either by nerve impulses or by increased extracelluar K+. When assessing glutamate and aspartate as potential transmitter compounds in preparations containing polysynaptic pathways, the findings suggest that results could be obtained from which misleading conclusions might be drawn. 23 references.

213279 Geller, Herbert M.; Woodward, Donald J. C.M.D.N.J.-Rutgers Medical School, Department of Pharmacology, P.O. Box 101, Piscataway, NJ 08854 **Responses of cultured cerebellar neurons to iontophoretically applied amino acids.** Brain Research (Amsterdam). 74(1):67-80, 1974.

Electrical activity of spontaneously firing neurons in explant cultures of neonatal rat cerebellum was recorded with extracellularly placed microelectrodes. Several different normal patterns of firing were noted, common ones being single spikes at regular intervals, irregularly spaced single spikes and rapid bursts of up to 10 spikes separated by periods of silence. The firing rate could be modified by the local application of drugs through iontophoresis onto the soma and adjacent processes. Firing rates were increased by glutamate and homocysteate, and decreased by gamma-aminobutyric acid (GABA) and glycine. The action of GABA was blocked by bicuculline and picrotoxin. GABA was relatively more effective than glycine. Acetylcholine was generally ineffective, but rarely had weak excitatory actions. It is concluded that the sensitivities of the cultured Purkinje cell with respect to these drugs is the same as the adult Purkinje cell in vivo and similar to the immature cell at the time of explantation. 33 references. (Author abstract modified)

213282 Abdallah, Abdulmuniem H.; Roby, Douglas M. The Dow Chemical Company, Chemical Biology Research, Midland, Michigan 48640 **Antagonism of depressant activity of ethanol by DH-524; a comparative study with bemegride, doxapram and d-amphetamine (38640).** Proceedings of the Society for Experimental Biology and Medicine. 148(3):819-822, 1975.

The effects of DH-524 (2(3,4-dichlorophenoxy)-methyl-2-imidazoline), bemegride, doxapram and d-amphetamine on the narcotic and hypothermic effect of ethanol in mice were examined. All doses of bemegride and doxapram tested failed to antagonize the effects of ethanol in spite of the fact that they caused convulsions in mice. Doxapram potentiated, rather than antagonized, the effects of ethanol in proportion to dose. It is concluded that DH-524 differs from all other agents tested in that it antagonized the pharmacological effects of ethanol in doses which produced no other pharmacological effects. 5 references.

04 MECHANISM OF ACTION: BEHAVIORAL

205628 Irmis, F. Psychiatric Research Institute, Prague 8, Bohnice, Czechoslovakia **Effects of scopolamine on the EEG of cortex and hippocampus during spontaneous behaviour in rats.** Activitas Nervosa Superior Praha). 16(3):220-222, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, reports an experiment designed to investigate the effects of scopolamine on the electroencephalogram (EEG) of cortex and hippocampus during spontaneous behavior in rats. Results suggest that hippocampal rhythmic slow activity (RSA) in wakeful rats under physiological conditions may be specifically related with the trunk and neck muscle activity. This muscle activity is involved in the behavior which may be called activated nonautomatized motor behavior, voluntary movements or exploratory activity. In other words, RSA may be a consequence of a certain activation in motor pathways and of proprioceptive reflexes. Even after anticholinergic and cholinergic drugs, the RSA remains essentially related to the above mentioned motor activity. The hippocampal arousal (RSA) in rats does not seem therefore to operate directly upon a cholinergic mechanism. 14 references.

205889 Davis, W. Marvin; Smith, Stanley G. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Central cholinergic influence on self-administration of morphine and amphetamine.** Life Sciences (Oxford). 16(2):237-246, 1975.

Atropine and methylatropine were tested in rats for an ability to alter the reinforcing action of intravenous morphine sulfate and d-amphetamine sulfate. Atropine blocked the self-administration of morphine, but methylatropine did not. Similarly, atropine but not methylatropine prevented the establishment of a conditioned reinforcer based on passive intravenous infusions of morphine. Self-administration of d-amphetamine was enhanced by atropine but not by methylatropine. Results indicate that a central cholinergic system exerts an influence on the brain mechanisms which are affected by morphine or d-amphetamine to produce positive reinforcement. 24 references. (Author abstract)

206086 Jacobs, Barry L.; Eubanks, Edwin E. Department of Psychology, Princeton University, Princeton, NJ 08540 **A comparison of the locomotor effects of 5-hydroxytryptamine and 5-hydroxytryptophan administered via two systemic routes.** Pharmacology, Biochemistry and Behavior. 2(1):137-139, 1974.

The effects of systematically administered 5-hydroxytryptamine (5-HT) and 5-hydroxytryptophan (5-HTP) on the tilt cage locomotor activity in rats are compared. 5-HT was a more potent inhibitor of activity than 5-HTP via both the s.c. and i.p. routes. The effect of 5-HT itself was greater when administered i.p.,and the effects of 5-HTP were independent of the route of administration. These results indicate that behavioral changes following 5-HTP injection may be attributable to the peripheral effects of 5-HT. 14 references. (Author abstract)

206109 Ksir, C. J. no address /**Scopolamine and amphetamine effects on discrimination.**/ no title. Final Report, NIMH Grant MH-23983, 1975, 3 p.

The effects of scopolamine, methylscopolamine, and d-amphetamine were studied in rats performing on three separate discrimination tasks. Both scopolamine and d-amphetamine interfered with stimulus control on a two key brightness discrimination task. These drugs also produced rate

dependent changes in responding on a multiple fixed interval extinction schedule such that low response rates were increased and high response rates were decreased by the drugs. Methylscopolamine tended to decrease responding in a nonrate dependent manner on the multiple schedule, and did not interfere with stimulus control in the brightness discrimination. The results indicate a similarity between rate dependent drug effects and effects on stimulus control of responding. (Author abstract)

206187 Franken, Robert E.; Strain, Allan. University of Calgary, Alberta, Canada **Effect of increased arousal on response to stimulus change in a complex maze.** Perceptual and Motor Skills. 39(3):1076-1078, 1974.

The effect of increased arousal on response to stimulus change in a complex maze was studied with 24 female and 24 male rats. They were tested under methamphetamine or saline in a six choice point multiple T-maze. On the first trial, the rats were exposed to a homogenous black or white maze. Between daily trials one and two, the maze was: a) left unchanged, b) the culs were changed from Black (B) to White (W) or W to B, or c) the path was changed from B to W or W to B. Findings indicate that methamphetamine treated rats made fewer approach responses to change when the change occurred in the culs and spent less time running from one end of the maze to the other. It is concluded that methamphetamine reduces the invitational properties normally associated with change or novelty. 6 references. (Author abstract modified)

206253 Panksepp, Jaak. Dept. of Psychology, Bowling Green State University, Bowling Green, OH 43403 **Effects of 2-desoxy-D-glucose on sleep-waking patterns.** Final Report, NIMH Grant MH-23945, 1975, 1 p.

Injections of 2-desoxy-D-glucose (250-750mg/kg) produce a dose dependent increase in cortical slow wave activity and decrease both paradoxical sleep and waking time in cats and rats. Insulin injections produced the same pattern of results. Accordingly, variations of glycolytic metabolism may participate in the control of sleep - waking behavior. Preliminary results indicate that inhibition of brain serotonin synthesis with para-chlorphenylalanine (200mg/kg daily) did not preclude elicitation of slow wave sleep with 2-desoxy-D-glucose, leading to the possibility that serotonin is not a necessary neurochemical substrate for slow wave sleep. (Author abstract)

206339 Takahashi, Ryo; Nagayama, Haruo; Kido, Atsuhiko; Morita, Takeki. Dept. of Neuropsychiatry, Nagasaki Univ. School of Medicine, Nagasaki, Japan **An animal model of depression.** Biological Psychiatry. 9(2):191-204, 1974.

A model of depression was produced in rats for the purpose of subsequent behavioral and biochemical studies. Using a conditioned reflex technique, a buzzer (conditioned stimulus) was paired with a tetrabenazine injection (unconditioned stimulus) for at least 11 trials. Following conditioning, the rats exhibited motionlessness after the presentation of the buzzer alone. Imipramine administration attenuated the conditioned motionlessness. 16 references. (Author abstract)

206355 Chesher, G. B.; Jackson, D. M. Dept. of Pharmacology, University of Sydney, Sydney, N.S.W. 2006, Australia **The effect of withdrawal from cannabis on pentylenetetrazol convulsive threshold in mice.** Psychopharmacologia (Berlin). 40(2):129-135, 1974.

The effect of withdrawal from cannabis or from ethanol upon the sensitivity of mice to pentylenetetrazol (PTZ) induced convulsions was investigated. Groups of mice were dosed with ethanol or cannabis extract for 11, 13 and 28 days. The threshold to convulsions produced by the constant intravenous infusion of PTZ was determined at various intervals after drug administration had ceased. The convulsive thresholds of mice tested 6 hours after withdrawal from two doses of alcohol were significantly lower than controls. There was no significant difference from controls in the convulsive threshold of mice which had received cannabis extract at any of the doses employed when tested 6 hours, 16 hours, 1, 3, or 6 days after medication had been withdrawn. Findings indicate there is no abstinence syndrome evident following withdrawal of cannabinoids after prolonged administration to mice and a distinction is demonstrated between cannabis and ethanol. 16 references. (Author abstract modified)

206358 Beecham, I. J.; Handley, Sheila L. Pharmacological Laboratories, Dept. of Pharmacy, University of Aston, Birmingham, England **Potentiation of catalepsy induced by narcotic agents during Haffner's test for analgesia.** Psychopharmacologia (Berlin). 40(2):157-164, 1974.

Potentiation of morphine catalepsy in the mouse during Haffner's (tail clip) test for analgesia was investigated. Very marked potentiation occurred in the presence of the clip. Both "native" and "clip" catalepsy were antagonized by nalorphine. Atropine antagonized morphine "native" catalepsy in a dose dependent fashion, but produced a parallel increase in both analgesia and "clip" catalepsy at higher doses. Haloperidol catalepsy was abolished in the presence of the clip but reappeared on its removal. Findings suggest that morphine must have at least two sites of action in producing catalepsy. 8 references. (Author abstract modified)

206439 Mil'shteyn, G. I.; Gyunter, M.; Lagutina, N. I.; Smirnova, L. B. Voyenno-meditsinskaya akademiya im. S. M. Kirova, Leningrad, U.S.S.R. **/The influence of chlorpromazine action on experimental psychosis caused by lysergic acid diethylamide./** Vliyaniye aminazina na eksperimental'nyy psikhoz, vyzvannyy dietilamidom lizerginovoy kisloty. Farmakologiya i toksikologiya (Moskva). 37(5):537-539, 1974.

The influence of chlorpromazine activity on the disturbances of higher neural activity triggered by lysergic acid diethylamide was investigated in dogs and apes. Intravenous doses of chlorpromazine elicited changes in the conditioned reflex activity of apes; the larger the dose, the more intense the response. Intramuscular injections of the same preparation, however, exerted no influence on neural disturbances in dogs. 18 references. (Journal abstract modified)

206440 Abuladze, G. V. Laboratoriya neyrofiziologii i farmakologii povedeniya, Instituta fiziologii Sibirskogo otdeleniya AN SSSR, Novosibirsk, U.S.S.R. **/The role of the reticular formation in action exerted by chlorpromazine and benactyzine on primary responses of the brain cortex./** Rol' retikulyarnoy formatsii v deystvii aminazina i amizila na pervichnyye otvety kory mozga. Farmakologiya i toksikologiya (Moskva). 37(5):539-542, 1974.

Reticular formation activity stimulated by chlorpromazine and benactyzine was investigated in nonanesthetized curarized cats. Intravenous injections of chlorpromazine were found to increase the amplitude of both the visual and somatosensory responses of the cortex, but they did not modify the responses of specific thalamic nuclei. No increase in the amplitude of responses was noted after severance of the reticular forma-

tion. Intravenous injections and local application of amizyl was found to intensify somatosensory responses in cats with premesencephalic sections and intact brains. 22 references. (Journal abstract modified)

206714 Thor, Donald H.; Ghiselli, William B. Edward R. Johnstone Training and Research Center, Bordentown, NJ 08505 **Suppression of mouse killing and apomorphine-induced social aggression in rats by local anesthesia of the mystacial vibrissae.** Journal of Comparative & Physiological Psychology. 88(1):40-46, 1975.

The influence of local facial anesthesia on mouse killing and spontaneous drug induced social aggression was investigated in rats. Known mouse killing rats were given bilateral lidocaine or placebo injections administered under ether anesthesia. Attack and kill latencies were significantly longer under lidocaine than under placebo; all subjects killed under placebo, whereas a third of all subjects failed to kill on the initial lidocaine test. On subsequent lidocaine testing, latencies decreased and nonkilling rats killed. Intense apomorphine induced conspecific fighting in rats preselected for aggressiveness was markedly reduced following lidocaine anesthesia. Comparative results of both experiments are interpreted in reference to theoretical assertions regarding the import of sensory information in stimulus bound attack and the typology of central aggression systems. 26 references. (Author abstract modified)

206724 Schwartzbaum, J. S.; Kreinick, Carol J. Dept. of Psychology, University of Rochester, Rochester, NY 14627 **Electrophysiological and behavioral reactivity to photic stimuli following septal lesions and pharmacological treatments in rats.** Journal of Comparative & Physiological Psychology. 88(1):128-146, 1975.

Lesion induced changes in reactivity to photic stimuli were examined in the rat to define the variation in behavioral and electrophysiological patterns of responses and to identify pharmacological properties of these varied patterns. Analysis of behavioral reactivity and cortical visual evoked response (VER) to stimulation revealed two patterns of lesion induced changes. One pattern of VERs reflected a hypoarousal electrophysiological condition, present initially under all conditions, which could be simulated with administration of scopolamine. A second pattern of VERs developed gradually and appeared to reflect a hyperaroused electrophysiological condition which could be simulated with d-amphetamine. While both lesion induced electrophysiological patterns were associated with augmented behavioral reactivity to flashes, the hyperarousal pattern related to more intense conditions of stimulation and more sustained behavioral reactivity. Scopolamine, as opposed to d-amphetamine, reproduced the heightened behavioral reactivity to the flashes. Results were interpreted in terms of a hypoarousal hypothesis of sensory hyperreactivity. 43 references. (Author abstract modified)

206727 Simpson, C. Wayne; Baile, C. A.; Krabill, L. F. Dept. of Psychology, SUNY, Brockport, NY 14420 **Neurochemical coding for feeding in sheep and steers.** Journal of Comparative & Physiological Psychology. 88(1):176-182, 1975.

Feeding responses of sheep and steers were compared following intraventricular injection of alpha-adrenergic agonists and antagonists in 2 hour tests. In sheep, injection of the alpha-agonist l-norepinephrine (l-NE) 1 increased feed intakes 288% and 388% compared with intakes following synthetic cerebrospinal fluid. This response was blocked by the alpha-antagonist phenoxybenzamine, whereas the antagonist alone decreased feed intake. The beta-adrenergic antagonist propranolol did not modify the l-NE response. A purer but weaker alpha-agonist l-phenylephrine also resulted in increased food intake that was blocked by phenoxybenzamine. In contrast, l-NE caused hypophagia in steers, reducing intakes as much as 58% in 2 hour tests. Phenoxybenzamine blocked the l-NE induced hypophagia in steers; when injected alone, it increased feed intake 181% of control values. Changes in feeding following l-NE injections are not attributed to changes in temperature, fat mobilization or stupor. 24 references. (Author abstract modified)

206733 Carey, Robert J.; Goodall, Edwin; Lorens, Stanley A. Veterans Administration Hospital, Irving Avenue and University Place, Syracuse, NY 13210 **Differential effects of amphetamine and food deprivation on self-stimulation of the lateral hypothalamus and medial frontal cortex.** Journal of Comparative & Physiological Psychology. 88(1):224-230, 1975.

The influences of motivational state and certain drugs on the intracranial self-stimulation phenomenon (ICSS) in rats was studied. ICSS of the lateral hypothalamus was markedly increased by d-amphetamine administration and by food deprivation. Similar self-stimulation response rates obtained in the same animals from the medial frontal cortex were unaffected by food deprivation and only slightly increased by d-amphetamine administration. Furthermore, a large difference between d-amphetamine and l-amphetamine on response rate was obtained for lateral hypothalamic but not for medial frontal cortex self-stimulation. Findings are consistent with a noradrenergic self-stimulation system for the lateral hypothalamus. However, medial frontal cortex self-stimulation appears to be mediated by a neuroanatomical and neurochemical system different from that of the lateral hypothalamus. 14 references. (Author abstract modified)

206739 Kelsey, John E. Dept. of Psychology, Indiana University, Bloomington, IN 47401 **Role of pituitary-adrenocortical system in mediating avoidance behavior of rats with septal lesions.** Journal of Comparative & Physiological Psychology. 88(1):271-280, 1975.

Three experiments examined the hypothesis that the effects of septal lesions and systemic injections of scopolamine on avoidance acquisition could be attributed to the effects of either of these treatments on adrenocorticotropic hormone (ACTH) secretion. Septal lesions and scopolamine facilitated two way conditioned avoidance response acquisition, and the lesions retarded passive-avoidance acquisition. However, neither the injections of dexamethasone, a synthetic glucocorticoid which inhibited ACTH secretions as did septal lesions, nor injections of ACTH secretion, affected avoidance in these paradigms. Thus, the main hypothesis was not supported. The finding that scopolamine did not affect passive-avoidance indicates that a cholinergic system may not be involved in mediating the suppressive effects of punishment. 27 references. (Author abstract)

206741 Leith, Nancy J.; Barrett, Robert J. Tennessee Neuropsychiatric Institute, Central State Hospital, Nashville, TN 37217 **Effects of hippocampal microinjections of d-amphetamine and scopolamine on active avoidance behavior in rats.** Journal of Comparative & Physiological Psychology. 88(1):285-299, 1975.

To obtain information on the role of the hippocampus in mediating the effects of d-amphetamine and scopolamine, the effects of both drugs in the dorsal and in the ventral portions of that structure were examined during an active avoidance task. Bilateral microinjections of scopolamine and d-

amphetamine were administered prior to each of eight daily training sessions in a discriminated Y-maze. Scopolamine, but not d-amphetamine, facilitated avoidance responding in both sites, with the effect being greatest following administration into the dorsal hippocampus. On days 9 and 10, all animals received saline injections and were tested for transfer of responding to the nondrug state. A decrement of performance occurred, irrespective of whether the drug had facilitated avoidance responding. The performance changes were greater following termination of scopolamine than d-amphetamine injections, and in no case were they as great as those previously reported following peripheral injections of the drugs. 50 references. (Author abstract modified)

206742 Vanderwolf, C. H. Dept. of Psychology, University of Western Ontario, London, Ontario, Canada **Neocortical and hippocampal activation in relation to behavior: effects of atropine, eserine, phenothiazines, and amphetamine.** Journal of Comparative & Physiological Psychology. 88(1):300-323, 1975.

Effects of various drugs on cerebral activation were investigated using the technique of slow wave recording in chronic animal preparations together with detailed observation of overt behavior of rats. Evidence suggests that the hippocampus receives two nonspecific inputs from the brainstem, each capable of producing rhythmical slow activity. The neocortex appears to receive two similar inputs, each capable of producing low voltage fast activity. One input to both hippocampus and neocortex is blocked by atropine and stimulated by eserine, and is essentially unrelated to concurrent motor activity. A second input to both hippocampus and neocortex is resistant to atropine, is depressed by phenothiazines, and is activated by d-amphetamine. Activity in this system is closely related to concurrent voluntary movement. 51 references. (Author abstract modified)

206745 Carlson, R. H.; Sanders, M. G.; Tal, A.; Wood, W. G. Dept. of Psychology, Texas Tech University, Lubbock, TX 79409 **Attentuation of "acute" habituation by scopolamine in the black-tailed prairie dog (Cynomys ludovicianus).** Journal of Comparative & Physiological Psychology. 88(1):335-341, 1975.

The hypothesis that scopolamine attenuates habituation occurring within a training session as well as that occurring between training sessions was tested in the prairie dog and confirmed. Scopolamine injections reduced spontaneous wheel running, but did not affect the threshold for wheel running induced by electrical brain stimulation (EBS). Another experiment demonstrated that EBS induced running declined during a 10 minute stimulation period and indicated that the decline was habituative since the response was repeatedly dishabituated. In a final experiment, scopolamine reduced habituation of EBS induced wheel running during 10 minute sessions. 21 references. (Author abstract modified)

206747 Glick, S. D.; Marsanico, R. G. Dept. of Pharmacology, Mount Sinai School of Medicine, Fifth Avenue and 100th St., New York, NY 10029 **Time-dependent changes in amphetamine self-administration following frontal cortex ablations in rats.** Journal of Comparative & Physiological Psychology. 88(1):355-359, 1975.

Changes in sensitivity to behavioral effects of amphetamines after lesions of frontal cortex were studied in rats trained to intravenously self-administer d-amphetamine during daily 1 hour testing sessions. Following removal of frontal cortex, rates of d-amphetamine self-administration were higher at early (3 to 5 days) postoperative intervals but lower at later (2 to 4 weeks) postoperative intervals. These and other results indicate that, as a function of time after surgery, frontal rats are first hyposensitive and then become increasingly hypersensitive to the rewarding effect of d-amphetamine. 13 references. (Author abstract modified)

206751 Nakajima, Shinshu. Dept. of Psychology, Dalhousie University, Halifax, Nova Scotia, Canada **Amnesic effect of cycloheximide in the mouse mediated by adrenocortical hormones.** Journal of Comparative & Physiological Psychology. 88(1):378-385, 1975.

The involvement of adrenocortical hormones in the amnesic effect of cycloheximide was examined in mice. Subcutaneous injection of cycloheximide shortly before a training trial of a passive-avoidance task resulted in an amnesia of the avoidance response. However, amnesia was absent in the adrenalectomized animals in which cerebral protein synthesis was suppressed by cycloheximide. Injection of corticosteroids antagonized the amnesic effect most effectively if the steroids were given immediately after training. The influence of the hormonal treatments upon the amnesic effect was not attributable to a change in general activity level. The amnesic effect of subcutaneously injected cycloheximide appears to be mediated by hormonal deficiency and does not seem related to suppression of the cerebral protein synthesis. 28 references. (Author abstract modified)

206752 Quartermain, David; Botwinick, Chaim Y. Dept. of Neurology, Milbank Laboratory, New York University School of Medicine, New York, NY 10016 **Role of the biogenic amines in the reversal of cycloheximide-induced amnesia.** Journal of Comparative & Physiological Psychology. 88(1):386-401, 1975.

In a study of the role of the biogenic amines in the reversal of cycloheximide (CYC) induced amnesia, amnesia was induced by pretraining injections of CYC in a food motivated discrimination reversal task. Magnitude of amnesia in mice varied as a function of amount of training on both the initial discrimination and the reversal and also as a function of the length of intertrial interval use on both the reversal and the test. Memory spontaneously recovered 48 hours following reversal training. Recovery from amnesia was induced by pretesting injections of d-amphetamine and two monoamine oxidase inhibitors, pargyline and catron. This enhanced performance was a true recovery of memory and not a result of enhanced learning or increased arousal. Depletion of catecholamines by alpha-methyl-para-tyrosine and diethyldithiocarbamate resulted in an amnesia quantitatively and qualitiatively similar to amnesia induced by CYC. Data support the hypothesis that CYC induced amnesia is mediated via central catecholamines. 45 references. (Author abstract modified)

206786 Niemegeers, C. J. E.; Van Nueten, J. M.; Janssen, P. A. J. Dept. of Pharmacology, Janssen Pharmaceutica, Research Laboratoria, Beerse, Belgium **Azaperone, a sedative neuroleptic of the butyrophenone series with pronounced anti-aggressive and anti-shock activity in animals.** Arzneimittel-Forschung (Aulendorf). 24(11):1798-1806, 1974.

The pharmacological profile of azaperone, in mice, rats, dogs and on isolated tissues is presented and compared with those of promazine, levomepromazine, chlorpromazine and haloperidol. Azaperone is a sedative neuroleptic of the butyrophenone series. Pharmacological results indicate qualitative similarities to levomepromazine, and quantitative advantages over the latter compound, such as more rapid onset of action, greater manageability and higher potency. Findings suggest that azaperone is a safe, sedative neuroleptic with out-

standing antiagressive and antishock activity. 27 references. (Author abstract modified)

206787 Chandra, O.; Bernard, J.; Matussek, N. Dept. of Pharmacology, J. N. Medical College, Aligarh Muslim University, Aligarh, India **Long-term trial of fluphenazine decanoate and flupenthixol decanoate for cataleptic activity and effect on motor activity in rats.** Arzneimittel-Forschung (Aulendorf). 24(11):1821-1824, 1974.

The cataleptic activity and the effect on motor activity and circadian rhythm of two long acting neuroleptics, fluphenazine decanoate and flupenthixol decanoate were tested in long-term experiments with rats. Both drugs showed dose dependent cataleptic activity. Fluphenazine decanoate was a significantly more potent cataleptic agent than fluphenthixol decanoate only in the first 24 hours. During this time fluphenazine decanoate was also a significantly more potent inhibitor of motor activity. Cataleptic activity and motor inhibitory activity of both compounds quickly dissociated after 24 hours; the latter returned to normal, while the cataleptic activity persisted for more than 40 days in the highest dose tested. It is suggested that the cataleptic activity may be used as a test for the preliminary screening of such compounds. 14 references. (Author abstract modified)

206836 Auriel, B.; Pinar, N.; Bord, M. no address /**Pindolol: a new psychotropic drug.**/ Le pindolol: un nouveau psychotrope. Encephale (Paris). 62(5):427-441, 1973.

The clinical results of a study on a new psychotropic drug, pindolol (Visken), are reported. Hypotheses were formulated based on these drugs' effects on subjects under stress, on general transformation under treatment from negative to positive anxiety and its effect on sleep. The population treated is described in terms of sex, drugs used, dosage, treatment duration, age and specific nosology. The tabulated results are analyzed on the basis of the drug's effects on the thymus, on activity, on contact, on anxiety, and its antidelerious and hallucinogenic character. Drug tolerance is described. It is concluded that pindolol can be used on melancholics or schizophrenics who do not react to classical treatments in order to release some of their fears. 43 references. (Author abstract modified)

207035 Garver, David L.; Schlemmer, R. Francis, Jr.; Maas, James W.; Davis, John M. Illinois State Psychiatric Institute, 1601 W. Taylor St., Chicago, IL 60612 **A schizophreniform behavioral psychosis mediated by dopamine.** American Journal of Psychiatry. 132(1):33-38, 1975.

Schizophrenic behavioral disturbances which were induced in members of a macaque social colony by the chronic administration of d-amphetamine were studied. Findings indicate that animals given the drug show hypervigilance, hyperactivity, fragmented and repetitive behaviors, and progressive social withdrawal as well as the development of solitary stereotypies. The syndrome was dissected pharmacologically with alpha-methyl-para-tyrosine, chlorpromazine, pimozide, and haloperidol. Based on the behavioral findings and the known mechanisms of action of these drugs, it is concluded that the major elements of the psychotic like behavior induced by d-amphetamine are mediated by dopamine systems. 12 references. (Journal abstract modified)

207163 Lyubimov, B. I.; Smol'nikova, N. M.; Strekalova, S. N. Institute of Pharmacology, U.S.S.R. Academy of Medical Sciences, Moscow /**The effect of diazepam on the development of progeny.**/ Vliyaniye diazepama na razvitiye potomstva. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 78(10):64-66, 1974.

The effect of introducing diazepam during pregnancy on progeny was investigated in female rats. Diazepam was introduced daily throughout pregnancy. Before giving birth, rats were placed in separate cages. The offspring were periodically weighed, and the reaction of their stomachs was observed. Spontaneous motor activity was measured weekly from 3 weeks old to attainment of sexual maturation. Rats whose mothers had been exposed to diazepam were found to be more emotional and to have a more well developed investigative instinct than the control group. The changes in behavior were apparently caused by the activating effect of the diazepam preparation on the fetus after penetration of the placental barrier. 12 references. (Author abstract modified)

207284 Randrup, A.; Munkvad, I. Sct. Hans Mental Hospital, Department E, DK-4000, Roskilde, Denmark **Pharmacology and physiology of stereotyped behavior.** Journal of Psychiatric Research (Oxford). 11:1-10, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the stereotyped feature of the behavior of amphetaminized animals was discussed. The psychology of stereotyped behavior was examined. The neuroleptics seem to influence each of the items of behavior changed by amphetamine, such as locomotion, rearing, various forms of grooming, social and operant activities, eating, and drinking. Each type of behavior, however, is influenced also by other brain systems; each item seems to be regulated by a mosaic of factors, dopamine being one of the components of the mosaic. Aggressive behavior increased by amphetamine can be strongly and specifically reduced by neuroleptics. Disruption of patterns of social activity in monkeys by amphetamine can to some extent, but not completely, be restored by neuroleptics. The hypothesis that absolute or relative overactivity of dopaminergic systems in the brain is an important feature in the etiology of schizophrenia should be considered. 73 references.

207287 Snyder, Solomon H. Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Stereoselective features of catecholamine disposition and their behavioral implications.** Journal of Psychiatric Research (Oxford). 11:31-39, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, steric features characterizing the release, reuptake, and receptor activation of catecholamines were discussed in terms of their behavioral implications. The postsynaptic receptor actions of norepinephrine but not of dopamine are strikingly stereospecific. A considerably lesser "steroselectivity" characterizes the presynaptic uptake and release properties of norepinephrine neurons in the peripheral sympathetic nervous system and in the brain. Dopamine nerve terminals display less stereoselectivity in their uptake mechanism. The differential stereoselectivity of dopamine and norepinephrine neurons has prompted the use of isomers of amphetamine in attempts to discern whether particular behaviors in animals are predominantly dopamine or norepinephrine mediated. In man, amphetamine isomers have been evaluated for central stimulant effects, production of amphetamine psychosis and exacerbation of schizophrenic symptoms. 40 references. (Author abstract modified)

207302 Fibiger, H. C.; Phillips, A. G. Division of Neurological Sciences, Department of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada **Role of dopamine and norepinephrine in the chemistry of reward.** Journal of Psychiatric Research (Oxford). 11:135-143, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the role of dopamine and norepinephrine in the chemistry of reward was examined. The vast majority of information regarding the selective action of haloperidol and pimozide on dopamine receptors is derived from the fact that by some feedback mechanisms, dopamine turnover is increased by dopamine receptor blockade. Clinical results suggest that there exist separate dopaminergic and noradrenergic systems in the brain which will support intracranial self-stimulation (ICS). ICS obtained from electrodes in the dorsal NA bundle is consistently decreased by small doses of haloperidol, suggesting that the functional integrity of certain dopaminergic systems is a prerequisite for maintenance of ICS regardless of location of the electrode. More fundamental knowledge regarding the neurophysiology of catecholamine neurons as well as the neuropsychopharmacology of amphetamine are needed. 52 references.

207306 Crow, T. J.; Gillbe, C. Division of Psychiatry, M.R.C. Clinical Research Centre, Northwick Park Hospital, Watford Road, Harrow, London, HA1 3uj **Brain dopamine and behaviour: a critical analysis of the relationship between dopamine antagonism and therapeutic efficacy of neuroleptic drugs.** Journal of Psychiatric Research (Oxford). 11:163-172, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, evidence concerning the functional role of the system of dopamine containing neurons arising from the ventral mesencephalon was summarized. On the basis of the histochemical evidence and the effects of electrical stimulation, it appears that the entire system of fibers arising from the A8, A9, and A10 areas of Dahlstrom and Fuxe may function as a single unit. The hypothesis is proposed that the dopamine system functions as a mechanism which mediates some of the effects of positively rewarding stimuli on the organism's behavior. The hypothesis that dopaminergic overactivity or "hyperarousal" underlies some components of schizophrenic dysfunction provides a possible explanation of the mode of action of neuroleptic drugs. 58 references. (Author abstract modified)

207486 Anderson, J. A. D.; Basker, M. A.; Dalton, R. Guy's Hospital Medical School, London, England **Migraine and hypnotherapy.** International Journal of Clinical and Experimental Hypnosis. 23(1):48-58, 1975.

Forty seven migraine sufferers were divided into two groups and were treated with either hypnosis or prochlorperazine. Treatment was followed by monthly assessments and independent evaluation of 1 year of continuous care. Criteria of improvement were the number of attacks per month, number who had Grade 4 attacks, and complete remission. Results show that both the number of attacks and the number who suffered blinding attacks were significantly lower for the group receiving hypnotherapy than for the group receiving prochlorperazine. 13 references. (Journal abstract modified)

207794 Creese, Ian; Iversen, Susan D. Department of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **The pharmacological and anatomical substrates of the amphetamine response in the rat.** Brain Research (Amsterdam). 83(3):419-436, 1975.

The pharmacological and anatomical substrates of the amphetamine response in the rat were examined, and it was found that bilateral 6-hydroxydopamine microinjections into the substantia nigra abolished both the locomotor and stereotypy responses to D-amphetamine in adult animals. The lesions resulted in a depletion of over 99% of striatal tyrosine hydroxylase activity as well as severe noradrenaline depletions. Lesion of the dorsal or ventral noradrenergic pathways resulted in similar noradrenaline depletions but with no effect on striatal tyrosine hydroxylase levels and without the concomitant blockage of the amphetamine response. The substantia nigra lesioned rats were behaviorally supersensitive to apomorphine and L-DOPA and did not show a locomotor response to cocaine. The substantia nigra lesioned rats were not aphagic or adipsic. It was concluded that both the locomotor and stereotyped responses induced by amphetamine are dependent on the functional integrity of the nigrostriatial dopamine pathway. 45 references. (Author abstract modified)

208617 Iturrian, W. B.; Johnson, H. D. Department of Pharmacology, University of Georgia, Athens, GA 30602 **Infantile auditory exposure and unusual response to antipsychotic drugs.** Proceedings of the Society for Experimental Biology and Medicine. 148(1):219-223, 1975.

Auditory exposure of infant mice as a cause of idiosyncratic response to antipsychotic drugs was examined. Reserpine and prochlorperazine were administered in separate experiments to adult mice and to adult hamsters that had recovered from audiosensitization induced by 30 seconds of doorbell sound during a critical period of infantile development. In contrast to controls that showed tranquilization in response to these drugs, the previously audiosensitized animals of both species responded with a high incidence of convulsive seizures. Possible mechanisms of the preconvulsant effects of reserpine and prochlorperazine are discussed. Idiosyncratic responses to antipsychotic drugs in adult laboratory animals are shown to result from infantile auditory exposure, and it is speculated that human idiosyncrasies to psychoactive drugs may be similarly based. 26 references. (Author abstract modified)

208991 Zin'kovskaya, L. Ya.; Komissarov, I. V.; Talalayenko, A. N. Kafedra farmakologii Donetskogo meditsinskogo instituuta, Donetsk, U.S.S.R. **/An analysis of monoaminergic mechanisms of the dorsal hippocampus which mediate the conditioned escape reaction in rats./** Analiz monoaminergicheskikh mekhanizmov dorsal'nogo gippokampa, realizuyushchikh uslovnuyu reaktsiyu izbeganiya krys. Byulleten' eksperimental'noy biologii i meditsiny (Moskva). 78(11):6-9, 1974.

Monoaminergic mechanisms of the dorsal hippocampus after local microinjections of dopamine, noradrenaline and serotonin were studied in rats. Doses of 5 micrograms failed to influence muscle tone and spontaneous motor activity, but prolonged the latnet period of the escape conditioned reflex. Inhibition of the reflex with dopamine was realized through neuron receptors sensitive to haloperidol alone. Noradrenaline effect was eliminated by alpha-adrenolytics. Etaperazine failed to alter the depressive effect of bioamines on the conditioned defense reflex, but noradrenaline significantly stimulated the motor activity of rats. Against the background of melipramine action, dopamine depressed the escape reaction and stimulated spontaneous motor activity, whereas noradrenaline under the same conditions caused depression of motor activity. 17 references. (Journal abstract modified)

209191 Uchimura, Hideyuki. no address **Aggression and neurotransmitters.** Clinical Psychiatry (Tokyo). 16(9):736-755, 1974.

The literature on the relationship between aggression and neurotran is reviewed. The relationship between aggression and catecholamines, serotonin, acetylcholine, gamma-aminobutyric acid, piperidine, hormone, and neurotransmitter balance is considered. 158 references.

209866 Iwahara, Shinkuro; Noguchi, Setsuko. Dept. of Psychology, Tokyo University of Education, 3-29-1 Otsuka, Bunkyoku, Tokyo 112, Japan **Effects of overtraining upon drug-state dependency in discrimination learning in white rats.** Japanese Psychological Research (Tokyo). 16(2):59-64, 1974.

In order to study the effects of overtraining on drug state dependency in discrimination learning, the drug protocol and/or training schedule was varied in four groups of rats. Saline and chlordiazepoxide were administered in four different sequences. All four groups were trained to criterion in a discrimination task, with one group allowed ten additional training days. Discrimination learning was slightly depressed by chlordiazepoxide. With state shifts, errors increased for all groups, but the overtrained group made fewer errors and attained criterion faster than other groups in the same drug state. It is concluded that overtraining produces more transfer to a different state and better retrieval with restored state. It is noted that dissociation or state dependency is measured not only in terms of lack of transfer or retrieval failure with a changed state but also in terms of complete retrieval with the recovered state. 9 references.

209897 Christy, Daniel; Reid, Larry. Bradley University, Peoria, IL 61606 **Methods of deconditioning persisting avoidance: amphetamine and amobarbital as adjuncts to response prevention.** Bulletin of the Psychonomic Society. 5(2):175-177, 1975.

In a study of methods of deconditioning persisting avoidance, rats were trained to avoid footshock in an automated one way avoidance box by climbing to a retractable ledge. After avoidance was well established (50 trials on three consecutive days), footshock was terminated. Groups then received response prevention (a forced stay on the grid by prolonged ledge retraction) under the influence of a placebo, one of two doses of amphetamine, or one of two doses of amobarbital. One group received no treatment. Three days after treatment procedures, Ss were tested for persistence of responding without further footshock. Response prevention by itself attenuated persisting responding compared to no treatment, and the only drug that further attenuated persisting responding was the low dose of amphetamine. 6 references. (Author abstract modified)

209951 Gold, Paul E.; Van Buskirk, Roderick B. Department of Psychobiology, School of Biological Sciences, University of California, Irvine, CA 92664 **Facilitation of time-dependent memory processes with posttrial epinephrine injections.** Behavioral Biology. 13(2):145-153, 1975.

The effect of posttraining epinephrine injections on memory storage processes is examined. Rats were trained with a weak footshock on a one trial inhibitory avoidance task. The animals received epinephrine injections immediately, 10 min, 30 min, or 2 hr after training. On a retention test 24 hr after training, animals which received subcutaneous injections of epinephrine immediately after training had retention performance which was significantly better than that of saline control animals. A lower or higher dose did not affect retention performance. Epinephrine injections given 10 min after training also significantly facilitated retention, but injections given 30 min or 2 hr after training did not affect retention. The findings suggest that the hormonal consequences of a training experience may normally modulate memory storage processes in untreated animals. 24 references. (Author abstract)

210325 Carlini, E. A.; Lindsey, Charles J. Departamento de Psicobiologia, Escola Paulista de Medicina, Rua Botucatu, 862, 04023, Sao Paulo, Brazil **Pharmacological manipulations of brain catecholamines and the aggressive behavior induced by marihuana in REM-sleep-deprived rats.** Aggressive Behavior. 1(1):81-99, 1974.

Studies were undertaken to verify whether pharmacological manipulations of brain dopamine (DA) and norepinephrine (NE) levels would interfere with the aggressive behavior induced by Cannabis sativa in rapid eye movement (REM) sleep deprived rats. A marihuana extract, apomorphine and amphetamine provoked in rats previously deprived of REM sleep for 96 hours an upright position with the animals pawing each other as in fighting. Nondeprived rats injected with drugs did not show this aggressive behavior. Haloperidol, chlorpromazine, alpha-methyl-p-tyrosine, and reserpine decreased the marihuana aggressiveness of the deprived rats. Increase of DA concentration by previous treatment with Dopa potentiated aggressiveness. Blockade of NE synthesis by FLA-63 was ineffective in reducing marihuana aggressiveness in deprived rats. It is suggested that in rats with neural excitability heightened by previous REM sleep deprivation, DA facilitates aggressive behavior, an effect inhibited by NE. This hypothesis would imply that marihuana induces aggressiveness in REM sleep deprived rats by inhibiting the central NE system through an as yet unknown mechanism. 37 references. (Author abstract modified)

210349 Poitou, P.; Boulu, R.; Bohuon, C. Laboratoire de Biologie Clinique et Experimentale, Institut Gustave-Roussy, 16 bis, Ave. Vaillant-Couturier, F-94800 Villejuif, France **Effect of lithium and other drugs on the amphetamine chlordiazepoxide hyperactivity in mice.** Experientia (Basel). 31(1):99-101, 1975.

The effect of lithium, tryptophan, 5-hydroxytryptophan, and p-chlorophenylalanine on amphetamine chlordiazepoxide hyperactivity was studied in mice. Prior administration of lithium, 5-hydroxytryptophan and tryptophan was shown to produce significant decreases in the drug induced anxiety. However, p-chlorophenylalanine had no effect. Results suggest that the simultaneous administration of dexamphetamine and chlordiazepoxide disturbs a norepinephrine - serotonin balance, and the disturbance might be prevented by lithium. This effect explains the action of lithium in mania. 28 references.

210351 Dorr, Marian; Steinberg, Hannah; Shapero, M. Dept. of Pharmacology, University College London, Gower St., London WC1E 6BT **Stimulation of sexual behaviour in rats by a benzodioxane derivative.** Experientia (Basel). 31(1):91-93, 1975.

The effect of WB-4371, a benzodioxane derivative, on sexual behavior was studied in rats and compared with effects of p-chlorophenylalanine (pCpA). Findings indicate that both substances markedly stimulated heterosexual activity in rats with a naturally low level of such activity; but rats showing a normal level of heterosexual behavior did not increase their levels with either WB-4371 or pCpA. Sexual activity produced by

both substances was blocked by administration of 5-hydroxytryptophan. 15 references.

210392 Rosenberg, Jordan; Woods, James H. Dept. of Psychology, California State Univ., Hayward, CA 94542 **Effects of pentobarbital on fixed-ratio discrimination.** Bulletin of the Psychonomic Society. 5(1):33-35, 1975.

The effects of pentobarbital on fixed-ratio discrimination was examined in pigeons. Doses in the range of 5 to 15mg/kg were administered to birds trained to respond under a fixed-ratio discrimination procedure. Pentobarbital administration produced a dose related reduction in the level of sensitivity of the discrimination between the two ratios. 4 references. (Author abstract modified)

210666 Sahakian, B. J.; Robbins, T. W.; Morgan, M. J.; Iversen, S. D. Department of Experimental Psychology, University of Cambridge, Cambridge, England **The effects of psychomotor stimulants on stereotypy and locomotor activity in socially deprived and control rats.** Brain Research (Amsterdam). 84(2):195-205, 1975.

Using measures of locomotor activity and stereotypy, dose response curves to several psychomotor stimulant drugs were obtained on rats reared in deprived or normal environments. At both 0.5and 1.5mg/kg d-amphetamine, the deprived rats exhibited more intense stereotyped behavior than the control rats. At 5.0mg/kg, both groups showed maximum response. There was no significant difference between the two groups in locomotor response. A similar pattern of results was found for pipradrol, cocain, and apomorphine. The findings show that different social and environmental experience can modify the response to dopaminergic stimulating agents. The results also suggest that stereotyped behavior should not be considered on the same continuum as locomotor activity. These two behaviors may be mediated by different mechanisms. 36 references. (Author abstract)

210667 Bateson, P. P. G.; Horn, G.; Rose, S. P. R. University of Cambridge, Sub-Department of Animal Behaviour, Madingley, Cambridge, England **Imprinting: correlations between behaviour and incorporation of (14C)uracil into chick brain.** Brain Research (Amsterdam). 84(2):207-220, 1975.

Correlations between behavior and incorporation of (14C)uracil into chick brain are presented. On the first day after hatching 106 domestic chicks were injected with (14C)uracil and exposed to a yellow or a red rotating flashing light for 72 min. Shortly before they were killed and 115 min after injection they were given a choice between the two lights. Incorporation of the (14C)uracil into four regions of the brain was measured. Differences between batches and between training conditions were eliminated as sources of variation by standardizing the behavioral and biochemical measures. Correlations between the measures were obtained. Chicks that were active from the early stages of training showed lower rates of incorporation in the midbrain, forebrain base and anterior roof of the forebrain than less responsive chicks. When the general lowering effect of behavioral activity on incorporation was eliminated as a source of variation, a striking positive correlation emerged between the preference for the familiar object and incorporation in the anterior forebrain roof. Since preference for the familiar is a direct measure of imprinting, and since no other behavioral measure is positively correlated with biochemical changes in anterior roof, it is concluded that these biochemical changes were closely linked with the learning process. 30 references. (Author abstract)

210671 Stein, Larry; Belluzzi, James D.; Wise, C. David. Wyeth Laboratories, Philadelphia, PA **Memory enhancement by central administration of norepinephrine.** Brain Research (Amsterdam). 84(2):329-335, 1975.

The consolidation of a passive-avoidance response by injecting a single dose of norepinephrine (NE) in the lateral ventricle of the rat brain immediately after the training trial is described. Every rat in the saline treated control group showed a substantial increase in response latency relative to that observed prior to shock training. Diethyldithiocarbamate (DDC) treated rats were amnesic. Administration of NE within 1 minute after shock training seemed to restore the long-term memory capacity of DDC treated rats to nearly normal levels. The results suggest that inhibition of NE biosynthesis during passive-avoidance training prevents long-term, but not short-term retention of the newly learned response. 34 references.

210674 Wenzel, J.; David, H.; Pohle, W.; Marx, I,; Matthies, H. Institut fur Anatomie de Bereiches Medizin, Charite, Germany **Free and membrane-bound ribosomes and polysomes in hippocampal neurons during a learning experiment.** Brain Research (Amsterdam). 84(1):99-109, 1975.

The ribosomes of the CA1 and CA3 pyramidal cells of the hippocampus were investigated by morphometric methods after the acquisition of a shock motivated brightness discrimination in rats. A significant increase in the total number of ribosomes was observed in CA1 cells of trained animals and in CA3 cells of both active controls and trained rats. A significant increase in membrane bound ribosomes was obtained in CA1 and CA3 cells after training only. The results confirm the suggestion of an increased protein synthesis in hippocampal neurons during and after the acquisition of a brightness discrimination. The results lead to the assumption that the protein synthesis in some neuronal cells may probably differ not only quantitatively, but also qualitatively in trained and untrained animals. 52 references. (Author abstract modified)

210704 Olds, M. E. California Institute of Technology, Division of Biology, Pasadena, CA 91109 **Effect of intraventricular norepinephrine on neuron activity in the medial forebrain bundle during self-stimulation behavior.** Brain Research (Amsterdam). 80(3):461-477, 1974.

The effect of norepinephrine (NE), dopamine and serotonin were studied on self-stimulation behavior and on the unit activity in the medial forebrain bundle (MFB) correlated with this behavior. It was found that all four substances facilitated self-stimulation behavior, but to different degrees and at different doses. L-NE was the most effective of the substances tested because it facilitated behavioral responding in a majority of the animals at each dose; D-NE was the least effective. The effects of dopamine and serotonin were facilitatory in some animals but not in others. Excitatory neuronal activity occurring during self-stimulation behavior in the MFB was reduced by L-NE, whereas inhibitory neuronal activity in the same pathway was potentiated. The significance of these results is discussed in terms of the view that NE could be one of the transmitters in the MFB and that its synaptic action there is likely to be inhibitory. 29 references. (Author abstract modified)

210708 Rogers, L. J.; Drennen, H. D.; Mark, R. F. Physiology Department, Monash University, Clayton, Victoria 3168, Australia **Inhibition of memory formation in the imprinting period: irreversible action of cycloheximide in young chickens.** Brain Research (Amsterdam). 79(2):213-233, 1974.

In a study of the inhibition of memory formation in the imprinting period, it was found that a single intracranial dose of cycloheximide administered during the first week of life renders a chicken permanently incapable of learning at its normal rate. The onset of the period of greatest sensitivity to cycloheximide's effect on subsequent visual learning is delayed until the end of the first day of life, just as is the critical period for visual imprinting. The time course of susceptibility for subsequent retarded auditory learning precedes that for visual learning in the same way that the ability to imprint in the auditory system precedes that for the visual system. The permanent learning deficit is not produced by brain mitochondrial protein synthesis inhibition using chloramphenicol and does not occur after subcutaneous injection of cycloheximide. Complete protection from the retardation effect has been conferred by manipulating early sensory experience while the drug is acting. The permanent learning deficit is a consequence of the effects, in the metabolically deranged brain, of the sensory input that is normally necessary for early learning. 38 references. (Author abstract modified)

210737 Freund, Gerhard. Veterans Administration Hospital and Department of Medicine, University of Florida, Gainesville, FL 32602 **Normal shuttle box avoidance learning after chronic phenobarbital intoxication in mice.** Psychopharmacologia (Berlin). 40(3):199-203, 1974.

The question of whether chronic sedation per se rather than specific effects of ethanol or its metabolites may be the cause of observed impairment of learning in rodents was examined. Mice consumed phenobarbital incorporated into liquid diets and maintained gross behavioral sedation and ataxia for 4 months. Three weeks after the discontinuation of phenobarbital in the diet, shuttlebox avoidance learning was not impaired in comparison with controls pair fed with a comparable phenobarbital free diet or laboratory chow ad libitum. Nonspecific sedation cannot explain the impairment of shuttlebox avoidance learning by chronic ethanol consumption previously demonstrated under comparable conditions. 10 references. (Author abstract)

210739 Siegel, R. K.; Brewster, J. M.; Jarvik, M. E. Department of Pharmacology and Psychiatry, University of California, Los Angeles, CA 90024 **An observational study of hallucinogen-induced behavior in unrestrained Macaca mulatta.** Psychopharmacologia (Berlin). 40(3):211-223, 1974.

An objective behavioral profile that could be used to distinguish the behavioral effects of hallucinogens from those of other classes of drugs was developed. Saline, bromolysergic acid diethylamide, and two doses each of lysergic acid diethylamide (LSD), diemethyltryptamine (DMT), chlorpromazine, and d-amphetamine sulphate were administered to solitary adolescent rhesus monkeys whose behavior was observed, videotaped, and scored in a number of categories. Hallucinogens (LSD and DMT) could be distinguished from other drugs by the increased frequency of unusual behaviors such as spasms, stereotypy, and inappropriate behavior, and the decreased amount of exploration time. Hallucinogens also produced distinctive qualitative changes in behavior. 40 references. (Author abstract)

210741 Dantzer, R.; Roca, M. I.N.R.A., Station de Pharmacologie, 180, Chemin de Tournefeuille, F-31300 Toulouse, France **Tranquilizing effects of diazepam in pigs subjected to a punishment procedure.** Psychopharmacologia (Berlin). 40(3):235-240, 1974.

The tranquilizing effects of diazepam in pigs subjected to a punishment procedure were examined. A punishment discrimination was conditioned in pigs by simultaneously rewarding with food and punishing with electric shock all operant responses made in the presence of an odorous stimulus. Suppression of the punished responses did not develop after 5 days of training in pigs chronically treated with diazepam. Diazepam consistently increased the number of punished responses on an already learned punished behavior and decreased the latency of the first response during and after the odorous stimulus signaling the shock contingency. 8 references. (Author abstract modified)

210742 Taylor, M.; Goudie, A. J.; Mortimore, Shelley; Wheeler, T. J. Department of Psychology, University College of North Wales, Bangor, Caernarvonshire, North Wales **Comparison between behaviours elicited by high doses of amphetamine and fenfluramine: implications for the concept of stereotypy.** Psychopharmacologia (Berlin). 40(3):249-258, 1974.

The behavioral effects of a range of high doses of D-amphetamine and DL-fenfluramine were investigated in rats. Subjects were observed individually for 1 min in every 5 for a period of 1 hour. The results indicate that both compounds induce abnormal behaviors, the latency of onset of which is directly proportional to dose. For both compounds an inverse correlation was found between normal and abnormal behaviors. The type of abnormal behavior observed differed considerably between drugs in that fenfluramine elicited backward walking and circling with no head swaying, over the dose range 10-30mg/kg; while the predominant abnormal behavior elicited by D-amphetamine, over the range 5-20mg/kg, was head swaying. At the highest doses of amphetamine used some backward walking was elicited, behavior which was totally absent at the lower doses. The implications of these results for the concept of stereotypy are discussed, and attention is drawn to an important distinction between abnormal and stereotyped behavior. 40 references. (Author abstract modified)

210743 Croze, S.; Bost, J. Laboratoire de Physiologie, VER Medicale Lyon Sud-Ovest, BP12, F-69600 Oullins, France **/Feeding behavior in sheep: effects of nialamide and 6-hydroxydopamine./** Comportement alimentaire du mouton: effets de la nialamide et de la 6-hydroxydopamine. Psychopharmacologia (Berlin). 40(3):259-268, 1974.

The effects of nialamide and 6-hydroxydopamine on feeding behavior in sheep were examined. Daily food intake, masticatory activity and reticular movements were studied in sheep before and after intracerebroventricular injections of various drugs. Four animals received nialamide and four others received 6-hydroxydopamine. Nialamide increased food intake in all the subjects. It increased rumination time and inhibited the oral reflex of the reticulum in half of the subjects. 6-Hydroxydopamine reduced food intake and rumination time and accelerated the rhythm of reticular contractions during rest and rumination. The effects of nialamide and 6-hydroxydopamine on the cerebral concentration of serotonin, noradrenaline and dopamine have been extensively documented over the past few years. Modifications of food intake, rumination and reticular motility can be explained by variations in the cerebral concentration of noradrenaline and/or dopamine. These two amines (or one of them) could be implicated in the control of rumination and could act on central mechanisms monitoring forestomach motility. 40 references. (Author abstract)

210748 Blundell, J. E.; Leshem, M. B. Psychology Department, Leeds University, Leeds LS2 9JT, England **The effect of 5-hydroxytryptophan on food intake and on the anorexic action of amphetamine and fenfluramine.** Journal of Pharmacy and Pharmacology (London). 27(1):31-37, 1975.

The effect of 5-hydroxytryptophan (5-HTP) on food intake and on the anorexic action of amphetamine and fenfluramine were examined. 5-HTP amphetamine and fenfluramine suppressed food intake in normal rats and in animals with lesions of the lateral hypothalamus. The anorexic effect of amphetamine was reduced in lesioned animals compared with controls while the effect of 5-HTP, like that of fenfluramine, was increased. When administered in conjunction with the anorexic drugs, 5-HTP markedly potentiated the anorexic effect of amphetamine in both control and lesioned animals. However, 5-HTP potentiated fenfluramine anorexia only in lesioned rats. These findings provide further evidence for the role of 5-hydroxytryptamine (5-HT), in the anorexic effect of fenfluramine, and suggest that a 5-HT mechanism, inhibitory for feeding, produces particualrly severe suppression of food intake in rats with lateral hypothalamic lesions. 34 references. (Author abstract)

210752 Gough, A. L.; Olley, J. E. School of Pharmacology, University of Bradford, Bradford BD7 1DP, West Yorkshire, England **Cannabis and amphetamine-induced stereotypy in rats.** Journal of Pharmacy and Pharmacology (London). 27(1):62-63, 1975.

The effect of cannabis on amphetamine induced stereotypy was investigated. The abnormal behavior patterns characteristic of amphetamine induced stereotypy: sniffing, rhythmic head and body movements, gnawing, licking and biting, were scored individually. After amphetamine alone the proportion and intensity of the stereotypy components is dose related, a low dose inducing a high level of sniffing with minimal signs of the other behavior patterns, higher doses however resulting in the reduction of sniffing and its replacement by an increase in the frequency and intensity of the mouth, head and body movements. Pretreatment with cannabis extract significantly modified the amphetamine induced behaviors in a dose dependent manner, reducing or abolishing the sniffing behavior and increasing the rhythmic head and body movements. Cannabis pretreatment, however, did not potentiate the gnawing, licking and biting behavior as would have been predicted if the effects were simple overall potentiation of amphetamine. 10 references.

210754 Costall, B.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, West Yorkshire, England **Serotonergic involvement with the stereotypy/catalepsy induced by morphine-like agents in the rat.** Journal of Pharmacy and Pharmacology (London). 27(1):67-69, 1975.

The effects of lesions placed in the medial or dorsal raphe nucleus on the catalepsy stereotypy induced by morphine sulphate (BDH), M6029 and M320 (N-(cyclopropylmethyl)-19-isopentylnororvinol hydrochloride) were examined in rats. Results indicate an important role for 5-hydroxytryptamine (5-HT) in the regulation of the behavioral effects of morphine like agents and emphasize the difference in the mechanisms concerned with stereotyped behavior induced by these agents and by the classicial dopmaine agonists (e.g. apomorphine, (+)-amphetamine). It is concluded that the ability of the amygdaloid lesion to modify the stereotypic effect of morphine like agents may be dependent upon interuption of its 5-HT mechanisms. The proposed amygdaloid - cataleptic: striatal - stereotypic balance may depend on 5-HT as well as dopamine mechanisms. 9 references.

210762 Doggett, N. S.; Reno, H.; Spencer, P. S. J. Department of Applied Pharmacology, Welsh School of Pharmacy, UWIST, Cardiff, Wales **The effect of drugs with antidepressant activity upon the hypothermia and behavioural depression induced in mice by pimozide or centrally administered noradrenaline.** Neuropharmacology (Oxford). 14(2):85-90, 1975.

The effects of drugs with antidepressant activity upon the hypothermia and behavioral depression induced in mice by pimozide or centrally administered noradrenaline were examined. The intraperitoneal injection of the dopamine receptor blocking agent pimozide produced, in mice, a marked behavioral depression which was associated with diminished locomotor activity, decreased responsiveness to external stimuli, slowed respiration, reduced muscle tone and hypothermia. Similar effects were produced by the introcerebroventricular injection of noradrenaline. In both cases, the depth of hypothermia provided an easily quantifiable measure of the extent of the behavioral depression and it was possible to classify representative examples of several categories of antidepressant into three distinct groups on the basis of their ability to antagonize this hypothermia. It is postulated that laboratory models of depression produced by the administration of pimozide or noradrenaline may help to define the pharmacological activity of antidepressants in terms of specific interactions with noradrenergic or dopaminergic pathways within the central nervous system. 24 references. (Author abstract)

210763 Brook, Cynthia; Iversen, Susan D. Department of Experimental Psychology, University of Cambridge, Downing Street, Cambridge, England **Changed eating and locomotor behaviour in the rat after 6-hydroxydopamine lesions to the substantia nigra.** Neuropharmacology (Oxford). 14(2):95-105, 1975.

Changes, eating and locomotor behavior were examined in the rat after 6-hydroxydopamine lesions to the substantia nigra. Bilateral 6-hydroxydopamine lesions to the substantia nigra of the rat result in 80-90% loss of striatal dopamine. In such animals, amphetamine does not induce stereotyped behavior but the running response to lower doses of amphetamine is unaffected. The lesion does, however, produce permanent changes in the spontaneous locomotor behavior of the rat. Aphagia was observed only in animals with greater striatal dopamine depletion which was associated with additional forebrain noradrenaline loss. 30 references. (Author abstract)

210783 Holtzman, S. G. Department of Pharmacology, Emory University, Atlanta, GA 30322 **Effects of nalorphine on avoidance behavior and locomotor activity in the rat.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 212(2):199-204, 1974.

Evidence that nalorphine increased avoidance responding and locomotor activity in the rat is presented. The magnitude of the stimulation of avoidance responding was directly related to the dose of nalorphine whereas an inverse relationship existed between drug dose and changes in locomotor activity. The effects of nalorphine on both behaviors were blocked by naloxone. It appears that these behavioral effects of nalorphine, unlike those of some other drugs with mixed agonist and narcotic antagonist properties, are mediated by a single morphine like component of action. 11 references. (Author abstract)

210784 Bassett, J. R.; Cairncross, K. D. School of Biological Sciences, Macquarie University, North Ryde, N.S.W. 2113, Australia **Effects of psychoactive drugs on responses of the rat to aversive stimulation.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 212(2):221-229, 1974.

In a study of the effect of psychotropic drugs on responses of rats to aversive stimulation, exposure of male rats to an irregular signalled footshock regimen induced extreme plasma corticosterone elevation. It is concluded that this degree of steroid elevation relates to a psychological component in the aversive situation. The effect of pentobarbital, diazepam, amitriptyline and chlorpromazine on steroid elevation was examined in acute (1 day) and chronic (4 day) situations. Escape performance was measured in the chronic situation. Results obtained demonstrate that all the drugs tested suppress escape performance in a dose dependant manner, and this performance deficit is accompanied by a reduction in steroid elevation in animals treated with diazepam, amitriptyline and chlorpromazine. Low doses of these drugs induced steroid reduction without suppressing escape latency. Adaptation occurred to these drug induced changes. The fact that certain drugs suppressed the steroid response at doses which produced no significant effect on escape behavior suggests that measurement of plasma steroid levels may be a more sensitive index of psychological involvement than the measurement of behavioral parameters. 25 references. (Author abstract)

210785 Karniol, I. G.; Takahashi, R. N.; Musty, R. E. Departamento de Psicobiologia, Escola Paulista de Medicina, Rua Botucatu, 862, 04023, Sao Paulo, Brazil **Effects of delta9-tetrahydrocannabinol and cannabinol on operant performance in rats.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 212(2):230-237, 1974.

In a study of operant performance, delta9-tetrahydrocannabinol (THC), cannabinol (CBN), or mixtures of these two drugs were administered to rats prior to performance of a fixed-interval task. THC produced depression of responses and reward frequency. The lowest dose of THC depressed response rate only. CBN depressed responses at the highest dose without affecting reward frequency. When the two drugs were combined, a dose related depression of responses and reward frequency occurred. CBN potentiated the effect of THC at one dose combination. THC and mixtures of the two drugs produced a depression of response rate during the entire 60 sec interval, while CBN depressed response rates in the first 30 sec following reward. CBN alone has a slight depressive effect on performance and may be either less potent or different in its effects on behavior. 17 references. (Author abstract)

210790 Lutz, M. P.; Domino, E. F. Department of Pharmacology, University of Michigan, Ann Arbor, MI 48104 **Some evidence for long term memory retention by orotic acid in rats bar pressing for water.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 211(1):123-127, 1974.

In a study of long-term memory, rats treated i.p. with either orotic acid or 0.9% NaCl for 3 days were trained to press for tap water reinforcement on a modified FR 30 schedule. They were subsequently removed from the testing situation for 2, 4, or 6 weeks and then retested to determine if orotic acid induced memory facilitation for FR 30 bar pressing behavior. Overall, there was a significant decrement in the 0.9% NaCl treated and the orotic acid treated animals. After single large doses of orotic acid, rats showed lethargy and a decrease in muscle tone with suppressed responding between 1 min and 86 min after injection. Wide individual variability was observed to these effects of the drug. Orotic acid by itself had no significant effect on water consumption. The long-term effects of orotic acid treatment in this study were very subtle, statistically significant at one time but not at another and sometimes in opposite directions. However, the overall grouped data indicated that the 3 day orotic acid treated animals showed less retention deficits than 0.9% NaCl treated controls. 6 references. (Author abstract)

210817 Squires, R. F. Research Laboratories, A/S Ferrosan, DK-2860 Soeberg, Denmark **Evidence that 5-methoxy-N,N-dimethyltryptamine is a specific substrate for MAO-A in the rat: implications for the indoleamine dependent behavioral syndrome.** Journal of Neurochemistry (Oxford). 24(1):47-50, 1975.

A simple method for the separation of 5-hydroxyindoleacetic acid (5 -HIAA) and 5-methoxyindoleacetic acid (5-MeOIAA) on columns of nonionic polystyrene (Amberlite XAD-2) is described. Administration of 5-methoxy-N, N-dimethyl-tryptamine (5-MeODMT) to rats results in a sixfold increase in brain 5-MeOIAA within 15 min. This increase is blocked by the selective inhibitor of monoamine oxidase-A, clorgyline, but not by the selective inhibitor of MAO-B, deprenyl, indicating that 5-MeODMT is deaminated almost entirely by MAO-A. It is concluded that very little 5-MeODMT or other 5-methoxyindoleamines are formed endogenously in rat brain and that the stereotyped syndrome of hyperactivity and tremors produced in rats by pretreatment with MAO inhibitors and L-tryptophan is dependent on the formation of an N-substituted derivative of 5-HT which is at least partly deaminated by MAO-B to 5-HIAA. 11 references. (Author abstract modified)

210853 Nagayama, Haruo; Kido, Atsuhiko; Morita, Takeki; Takahashi, Ryo. Department of Neuropsychiatry, Nagasaki University School of Medicine, Japan **A study of an animal model of depression by the conditioned reflex technique.** Clinical Psychiatry (Tokyo). 16(10):863-869, 1974.

An animal model of depression created by conditioned reflex technique in Wistar rats is discussed. Rats given tetrabenazine or saline solution intraperitoneally under noise stimulus showed an extreme amount of movement followed by a state of repose. This repose, the conditioned reflex, was partially eliminated by treatment with imipramine prior to presentation of the noise stimulus. The repose state is considered an animal model of depression. 15 references.

210860 Stinnette, Mary J.; Isaac, Walter. Department of Psychology, University of Georgia, Athens, GA 30602 **Behavioral effects of d-amphetamine and caffeine in the squirrel monkey.** European Journal of Pharmacology (Amsterdam). 30(2):268-271, 1975.

The behavioral effects of d-amphetamine and caffeine in the squirrel monkey were examined. Four squirrel monkeys were trained on a bar press response with reinforcement available every 80 sec. The effects of d-amphetamine and caffeine upon this response were studied in both light and dark. In addition to differential drug effects it was found that both illumination and sex of the subjects were important variables. 12 references. (Author abstract)

210861 Fibiger, Hans C.; Zis, Athanasios P.; Phillips, Anthony G. Department of Psychiatry, University of British Columbia, Vancouver, British Columbia, Canada **Haloperidol-induced distruption of conditioned avoidance responding: attenuation by prior training or by anticholinergic drugs.** European Journal of Pharmacology (Amsterdam). 30(2):309-314, 1975.

In a study of haloperidol induced disruption of conditioned avoidance responding, rats injected daily with haloperidol failed to acquire a one-way active avoidance response over a 9 day period. When these animals were subsequently tested without haloperidol, on the first drug free day they performed as well as animals given saline throughout the training period and significantly better than naive saline treated animals on the first day of training. The performance of rats which were trained for two days before receiving haloperidol was only partly blocked by the drug, while animals trained for 9 days before drug administration were immune to the disruptive effects. Three anticholinergic (muscarinic) drugs, atropine scopolamine and benztropine significantly reversed the effect of haloperidol on the acquisition of the avoidance response. The nature of the avoidance deficit produced by these treatments is discussed with reference to the possibility that they selectively block the initiation of voluntary motor responses. 34 references. (Author abstract modified)

210886 Tessel, Richard E.; Woods, James H.; Counsell, Raymond E.; Lu, Matthias. Department of Pharmacology, University of Colorado Medical Center, Denver, CO 80220 **Structure-activity relationships between meta-substituted N-ethylamphetamines and locomotor activity in mice.** Journal of Pharmacology and Experimental Therapeutics. 192(2):310-318, 1975.

The effects of N-ethylamphetamines substituted at the meta position of the phenyl ring with H, F, Cl, Br, I, CF3, CH3O, NO2 or OH were examined on locomotor activity in mice. With the exception of meta-CF3-N-ethylamphetamine (fenfluramine), all compounds stimulated locomotor activity to varying amounts as determined in dose activity curves that included doses which were ineffective through doses which either decreased activity relative to lower doses or were lethal. Analyses indicated that the extent to which these compounds increased locomotor activity was inversely related to meta substituent steric effects, whereas hydrophobic and electronic substituent effects did not contribute significantly to this relationship. In mice pretreated with pargyline, the stimulant effects of these compounds were potentiated and again were inversely related only to substituent size. In reserpine pretreated mice, no relationship was obtained with size, hydrophobic or electronic effects individually or together. Reserpine pretreatment eliminated the rate increasing effects of the iodinated and hydroxylated derivatives but not those of the other compounds. 20 references. (Author abstract modified)

210889 Hoffmeister, Friedrich. Institut fur Pharmakologie der Baterag, Postfach 130105, West Germany **Negative reinforcing properties of some psychotropic drugs in drug-naive rhesus monkeys.** Journal of Pharmacology and Experimental Therapeutics. 192(2):468-477, 1975.

The negative reinforcing properties of some psychotropic drugs in drug naive rhesus monkeys were examined. Rhesus monkeys, previously trained to avoid electric shock, pressed a lever to extinguish a light associated with an intravenous drug infusion scheduled to occur 30 seconds after the onset of the light. Each response when the light was on terminated the light for a 1 minute time out period (avoidance); a response during the infusion terminated the infusion (escape). Under these conditions the monkeys tolerated a high number of saline infusions. Saline was replaced by different doses of chlorpromazine, lysergic acid diethylamide (LSD) and pentobarbital each for six successive daily 2 hour sessions. Infusions of chlorpromazine or LSD generated and maintained avoidance/escape behavior, whereas most of the infusions of pentobarbital were tolerated. In rhesus monkeys with no previous drug experience, chlorpromazine and LSD, but not pentobarbital, have negative reinforcing properties. 14 references. (Author abstract)

210894 Rolinski, Zbigniew; Scheel-Kruger, Jorgen. Department of Pharmacology, Agricultural College, Lublin, Academicka 12, Poland **The effect of dopamine and noradrenaline antagonists on amphetamine induced locomotor activity in mice and rats.** Acta Pharmacologica et Toxicologica (Kobenhavn). 33(5-6):385-399, 1973.

The effect of noradrenaline antagonists, aceperone, phenoxybenzamine and dihydroergotamine and neuroleptic drugs with dopamine receptor blocking properties, i.e. haloperidol, perphenazine, trifluoperazine, spiramide and pimozide, was tested on the locomotor and rearing activity induced by amphetamine, 2.5mg/kg, in rats. In general it was found that the neuroleptic drugs in very low doses, haloperidol, 0.10mg/kg; perphenazine, 0.05mg/kg; trifluoperazine, 0.15mg/kg; spiramide, 0.05mg/kg and pimozide, 0.15mg/kg produced complete inhibition of the amphetamine activities, whereas much higher doses of aceperone, 20mg/kg and phenoxybenzamine, 20mg/kg only produced partial antagonism. Dihydroergotamine produced no significant effect on the amphetamine locomotor and rearing activity. The results indicate that the locomotor effect in mice and rats after amphetamine is dependent on both dopaminergic and noradrenergic mechanisms. Dopamine was regarded as most significant, since the amphetamine motility only seems possible in the presence of functional active dopamine receptors. 42 references. (Author abstract modified)

210899 Gianutsos, Gerald; Lal, Harbans. Department of Pharmacology and Toxicology, College of Pharmacy, University of Rhode Island, Kingston, RI 02881 **Aggression in mice after p-chloroamphetamine.** Research Communications in Chemical Pathology and Pharmacology. 10(2):379-382, 1975.

Aggression was observed in mice after p-chloroamphetamine (PCA) injection. Two or 3 days after a single high dose of PCA, aggression was reliably observed in male mice. This aggression was not produced when the same dose of d-amphetamine was injected or when PCA was injected 1 hour before testing. PCA produced an increase in locomotor activity 1 hour, but not 24 hours, after injection. 11 references. (Author abstract)

210916 George, Grizelda; Mellanby, Jane. Department of Experimental Psychology, University of Oxford OXI 3PS, England **A further study on the effect of physostigmine on memory in rats.** Brain Research (Amsterdam). 81(1):133-144, 1974.

The observation of Deutsch that the injection of the anticholinesterase DFP, dissolved in peanut oil, into the hippocampus of rats facilitated recall of a task which had been forgotten by control animals (given the peanut oil alone) was examined. The amnesia in such control animals was found not to be natural forgetting but resulted from the peanut oil injections themselves. Such injections given 24 h previously also impaired initial learning (although once a task has been learned under such conditions it is well-remembered a week later). The amnesia caused by the peanut oil injections was not counteracted by intraperitoneal injection of the more specific anticholinesterase, physostigmine. The findings do not support Deutsch's conclusion that changes in cholinergic function are involved in the natural decay of memory with time. 19 references. (Author abstract)

210930 Schoenfeld, Ronald I.; Neumeyer, John L.; Dafeldecker, William; Roffler-Tarlov, Suzanne. Behavioral Pharmacology Laboratory, Squibb Institute for Medical Research, Princeton, NJ 08540 **Comparison of structural and stereoisomers of apomorphine on stereotyped sniffing behaviour of the rat.** European Journal of Pharmacology (Amsterdam). 30(1):63-68, 1975.

A comparison of structural and stereoisomers of apomorphine (APO) on stereotyped sniffing behavior of the rat is presented. N-n-propylnorapomorphine (NPA) is 35 times more potent than APO in producing stereotyped behavior in rats. The effect of NPA is blocked by perphenazine but unaltered by alpha-methyltyrosine pretreatment and is accompanied by a decrease in central dopamine turnover. The activity of APO and NPA appears to be primarily in the (-)-isomer, and is diminished but not lost by removal of either hydroxyl group from the catechol ring system. 22 references. (Author abstract)

210931 Lal, Harbans; Colpaert, Francis C.; Laduron, Pierre. Department of Pharmacology, University of Rhode Island, Kingston, RI 02881 **Narcotic withdrawal like mouse jumping produced by amphetamine and L-dopa.** European Journal of Pharmacology (Amsterdam). 30(1):113-116, 1975.

Narcotic withdrawal like mouse jumping produced by amphetamine and L-Dopa is described. Upward jumping in mice that resembled the narcotic withdrawal syndrome was produced by a combination of amphetamine and L-Dopa administration. Neither drug alone caused that jumping. Pretreatment with haloperidol or pimoxide but not with phentolamine effectively blocked amphetamine - Dopa jumping. After Dopa there was an increase in the brain levels of Dopa, dopamine and norepinephrine. Amphetamine, ineffective in itself, enhanced Dopa induced elevation of brain Dopa and dopamine without affecting brain norepinephrine levels. 11 references. (Author abstract)

211068 Papeschi, R. Research Laboratory, Sct. Hans Hospital, Department E, Roskilde 4000, Denmark **An investigation on the behavioral and hypothermic effects of yohimbine: interaction with drugs affecting central and peripheral monoamines.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 208(1):61-80, 1974.

The hypothermia and the behavioral changes induced by yohimbine in the rat were investigated by studying the interaction of this alkaloid with various drugs which affect central and peripheral monoamines. The results indicated that hypothermia mainly stems from a peripheral blocking action of yohimbine on alpha adrenergic receptors, but a central component, through stimulation of serotonin receptors, may also exist. Yohimbine antagonized the aggressiveness and the increased locomotion induced by various drug treatments, such as pargyline + Ro4-4602 + L-Dopa, thus suggesting that this alkaloid blocks central noradrenaline mechanisms too; on the other hand, only the stereotyped activity induced by (+)-amphetamine was reduced by yohimbine, whereas that following apomorphine or Ro-4602 + L-Dopa was unaffected. This observation suggests that yohimbine may also disturb the intraneuronal metabolism of brain dopamine, though being inactive on dopamine receptors. 28 references. (Author abstract modified)

211219 Sdino, Ciro; di Prospero, Beatrice. Istituto di Psicologia, Facolta di medicina e Chirurgia, Universita cattolica S cuore, Rome /**Estrogen stimulations during neonatal period and their effects on emotional and operative behavior in the adult.**/ Stimolazioni di estrogeni durante il periodo neonatale e loro effetti sul comportamento emotivo ed operativo dell adulto. Archivio di Psicologia Neurologia e Psichiatria (Milano). 34(5):450-460, 1973.

In order to study the long-term influences of sexual hormones on female rats, 45 female rats were divided into three groups. One groups (hypo) was spayed, while the other two groups received regular injections of beta-stradiol estrogens beginning at age 4 days. On day 21 of the experiment the groups were subjected to three tests: a motility test, a shuttlebox test, and an open field test. Results show that the neonatal administration of estrogens influenced sensitivity and emotional development of the female rats, but the absence of estrogen due to spaying did not in any sense alter behavior. 19 references.

211511 Lewis, Michael J.; Margules, D. L.; Ward, O. Byron, Jr. Dept. of Psychology, Tufts University, Medford, MA 02155 **Opioid-reinforced operant behavior: selective suppression by alpha-methyl-para-tyrosine.** Journal of Comparative & Physiological Psychology. 88(2):519-527, 1975.

The effect of oral consumption of opioids on reinforcement of operant behavior was studied, and the relapse phenomenon observed in addicted individuals was examined. Morphine addicted rats performed operant bar press responses for opioid or milk rewards. When rats were then denied access to opioids, abstinence symptoms developed. Responding under extinction conditions 2 weeks after opioid withdrawal provided a measure of the "relapse" tendency. Systematic administration of DL-alpha-methyl-para-tyrosine, an inhibitor of catecholamine synthesis, suppressed these responses if they had been reinforced by an opioid but not if they had been established with milk reinforcement. This indicates that the integrity of the catecholamine systems is vital for relapse to occur. 20 references. (Author abstract modified)

211512 Tarpy, Roger M.; Augenbraun, C. B.; Holman, William L. Dept. of Psychology, Bucknell University, Lewisburg, PA 17837 **Hypothalamic self-stimulation in rats following immunosympathectomy or central nerve growth factor antiserum injection.** Journal of Comparative & Physiological Psychology. 88(2):528-533, 1975.

The central effects of nerve growth factor (NGF) antiserum injections were studied in two experiments to determine possible changes in catecholamine activity. It was hypothesized that if immunosympathectomized rats are deficient in central catecholamines, they would respond much less for hypothalamic stimulation relative to controls, and that this effect would be most apparent during a partial reinforcement schedule. Immunosympathectomized rats self-stimulated at a much lower rate on high variable ratio schedules of reinforcement than injected controls. No differences were found for responding on continuous reinforcement or low variable ratio reinforcement schedules. In the second experiment, a similar reduction in variable ratio response was found for subjects centrally injected with NGF antiserum relative to controls. Results suggest a reduction in central catecholamine levels as a results of antiserum treatment. 20 references. (Author abstract modified)

211538 Ritter, Sue; Wise, C. David; Stein, Larry. Dept. of Physiology and Pharmacology, College of Veterinary Medicine, Washington State University, Pullman, WA 99163 **Neurochemical regulation of feeding in the rat: facilitation by alpha-noradrenergic, but not dopaminergic receptor stimulants.** Journal of Comparative & Physiological Psychology. 88(2):778-784, 1975.

In a study designed to determine more precisely the relative effectiveness of norepinephrine (NE) and dopamine (DA) receptor stimulation in the facilitation of feeding, rats ate voraciously after intraventricular injections of the alpha-noradrenergic receptor stimulant clonidine. Intraventricular administration of l-NE also facilitated feeding, but similar injections of DA and apomorphine (a DA receptor stimulant) were ineffective and even tended to suppress feeding. Clonidine was 100 times more potent than NE and increased the intake of both the ordinary diet of powdered food and a highly palatable wet food. The anorexic action of amphetamine was reversed by centrally administered clonidine. In relation to noradrenergic mechanisms, feeding appears to be a respondent which is sensitized or disinhibited by activation of alpha noradrenergic receptors, rather than an operant which is reinforced by the release of NE. 26 references. (Author abstract modified)

211781 Phillips, Jimmie Mac. University of Houston **Effects of drug-altered serotonin levels on the acquisition of a shuttle-box avoidance task. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-1035 HC$13.50 MF$5.00 82 p.

The effects of drug altered levels of brain serotonin on active shuttlebox avoidance behavior were investigated. Parachlorophenylalanine (PCPA) treatments resulted in subjects which are hypersensitive to intense painful stimulation and less "emotional" and thus show more locomotor activity with intense stimulation. Locomotor activity with low levels of stimulation does not seem to be significantly affected by PCPA treatments. (Journal abstract modified)

211883 Centa, David Michael. Auburn University **The effects of strain, drug, and dose level on general activity and exploratory behavior in mice. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-553 HC$13.50 MF$5.00 102 p.

The interactive effects of pentobarbital, meperidine, dextroamphetamine, and ethanol administered at four dose levels to three different strains of mice were determined. Pentobarbital was associated with the highest levels of exploratory behavior, while dextroamphetamine induced the lowest levels. Generally, no significant differences were found in the residual quantity of a drug between the two kinds of tissues or between dose levels of a drug. No significant relationships were found between the residual quantity of drug in the tissues and the corresponding behavioral measurements. (Journal abstract modified)

211899 Gustafson, Linda Kaye Watland. University of Minnesota **Intraventricular amphetamine self-administration in the albino rat. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-197 HC$13.50 MF$5.00 153 p.

Naive albino rats were found to initiate self-administration for intraventricular doses of d-amphetamine; under chronic administration conditions, the rats showed alteration in rate of drug intake and weight loss associated with high drug intake. The rate of drug intake increased as dose increased in an approximately linear manner. Comparison of intraventricular with intravenous administration of d-amphetamine suggests that intraventricular d-amphetamine injections may reach the site of action involved in maintaining self-administration by an indirect route rather than by acting directly on a periventricular site. (Journal abstract modified)

212523 Polifko, Marie Louderback. Georgetown University **Effects of psychotropic drugs on extinction-induced aggression. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-26435 HC$13.50 MF$5.00 180 p.

The acute and chronic effects of pentobarbital, phenobarbital and d-amphetamine on the aggressive behavior of pigeons were assessed. The baseline procedure was a two component multiple schedule of food reinforcement composed of alternating cycles of continuous reinforcement (CRF) and extinction. Total number of mirror responses (aggression), time spent in the presence of the discriminative stimulus associated with food reinforcement during the CRF component, and total number of keypecks during the extinction component were recorded. The dose effect data indicate that aggressive behavior was generally more sensitive to the acute effects of all three drugs than keypecking behavior. Upon repeated administration of the same dose of the drug over a period of 20 to 30 days, tolerance gradually developed to the effect of phenobarbital to decrease aggression, but pentobarbital induced decreases were sustained. Tolerance developed to amphetamine related increases in aggression but not to decreases in aggression. Development of tolerance to the behavioral effects of the drugs was selective for certain behaviors. Findings suggest that the technique of schedule induced attack on a mirror offers several advantages over previously used methods for studying drugs and aggression. (Journal abstract modified)

212677 David, Fredegusto G. Temple University **Effects of d-amphetamine and pre-session shocks on Sidman avoidance with a tone in rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-28342 HC$13.50 MF$5.00 187 p.

The effects of d-amphetamine and presession shocks on Sidman avoidance in rats were investigated using a tone as the warning stimulus. In experiments one and two, pairing of the tone impaired acquisition of the response when the pairing was begun early in conditioning. As suggested, particularly in experiment three, the tone facilitated the response when its pairing was begun later in conditioning when the response was already stable. Electric shocks, freely and noncontingently delivered prior to each avoidance session induced similar bidirectional effects to a greater extent. Less similarly, a 0.5mg/kg dose of dextroamphetamine also induced such effects. Findings also showed that after acquisition, noncontingent presession shocks facilitated responding early within sessions and that the 0.5mg/kg dose of dextroamphetamine disrupted responding early within sessions. The effects of presession shocks and the drug were to cancel out each other. The simplicity and sufficiency of a descriptive and functional analysis of avoidance behavior were demonstrated. (Journal abstract modified)

212963 Ageel, Abdulrahman Mohamed. University of Arizona **The comparative effects of morphine and chlorpromazine on the acquisition of conditioned avoidance response. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-4939 HC$13.50 MF$5.00 47 p.

The acute effects of morphine sulfate and chlorpromazine hydrochloride on acquisition in rats of conditiond avoidance response (CAE) in a two way shuttlebox were studied in three experiments that represented three levels of difficulty. Relative difficulty was validated by observing that control Ss had progressively poorer rates of CAR acquisition with successively more difficult tasks. Naive rats were subjected to 60 massed

trials, which constituted the acquisition session. Results with morphine showed a biphasic response. Low doses exerted no effect on acquisition; intermediate doses enhanced acquisition; and high doses disrupted acquisition. Increasing task difficulty increased doses required to enhance acquisition Also, a dose that completely inhibited acquisition in a less difficult task enhanced it in a more difficult task. Doses that enhanced acquisition suppressed intertrial crossings acquisition of CAR and intertrial crossings. Generally, increasing the dosage resulted in more suppression of acquisition. (Journal abstract modified)

212964 Bailey, Paul Timothy. Howard University **Actions and interactions of abused drugs of the reward system. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-2797 HC$13.50 MF$5.00 125 p.

The effect of abused and addicting drugs, such as delta9-tetrahydrocannibinol (THC), the major psychoactive constituent of marihuana, mescaline, morphine, cocaine, and amphetamine, on the reward system was examined using an intracranial electric self-stimulation schedule in rats. Interactions between morphine and nalorphine and that of cocaine, amphetamine, and alpha and beta adrenergic blocking agents were further studied. Rats were stereotaxically implanted with bipolar stainless steel electrodes in their posterior lateral hypothalamus and trained to press a lever in a Skinner box for electric self-stimulation. Overall findings suggest that the effects of these drugs on the reward system can be correlated with their effects on the central nervous system (CNS). The CNS depressants such as delta9-THC, mescaline, and morphine caused a decrease in self-stimulation responding, whereas the stimulants such as cocaine and amphetamine caused facilitation of the responding. Thus, the technique of self-stimulation cannot be used to indicate the abused potential of a drug. (Journal abstract modified)

213030 Dempsey, George Lee. Louisiana State University and Agricultural and Mechanical College **Melanocyte-stimulating hormone: some behavioral effects. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-1920 HC$13.50 MF$5.00 70 p.

Naive male hooded rats received a mild electric shock after stepping down from a small wooden platform to test the behavioral effects of melanocyte stimulating hormone (MSH). After this trial, no animal was tested for 2 days. On the fourth day, all Ss were returned to the platform and their step down latencies recorded. Ss were injected with MSH, an MSH release inhibiting factor (MIF), or saline on acquisition day only, on extinction day only, on both days, or on all 4 days. Regardless of when MSH was injected, it increased resistance to extinction. Results obtained with this modified procedure confirm that MSH produces increased resistance to extinction and extend these findings to a pigmented strain of rats. A second study determined specific behavioral effects for various dosages of both MSH and MIF. The procedure was the same except all Ss were injected once daily for 4 days. (Journal abstract modified)

213131 Delfini, Leonidas Ferdinand, Jr. University of Denver **The effects of intravenous and subcutaneous epinephrine administration on conditioned suppression. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-4179 HC$13.50 MF$5.00 135 p.

The effects of epinephrine (EPI), which intensifies the sympathetic arousal often found to accompany such emotions as fear and rage, on fear mediated conditioned suppression in rats were assessed. The conditioned suppression or conditioned emotional response (CER) paradigm encompassed three phases, and each groups was further subdivided into three drug treatment groups: EPI administered subcutaneously (SQ) to increase baseline sympathetic arousal (SA) over the conditioning session, EPI administered intravenously (IV) to increase the sympathetic response to the UCS, and administration of saline injections both SQ and IV (Placebo control). Throughout CER training, heartrate (HR) measures were taken to monitor the effects on SA. The final phase was suppression testing. Findings showed that relative to placebo controls, either of the EPI injections produced increases in suppression, even though HR measures showed that EPI produced reliable increases in SA. Findings are discussed in terms of measurement sensitivity and the appropriateness of EPI relative to alternative methods such as SA blockade, for testing SA effects on fear. (Journal abstract modified)

213153 Klipec, William David. University of Arizona **The effects of dextro-amphetamine monophosphate on the peak shift. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-4134 HC$13.50 MF$5.00 35 p.

The effects of dextro-amphetamine monophosphate on the peak shift of pigeons were examined to further assess previous observations that the peak shift is sensitive to the effects of chlorpromazine and delta9-tetrahydrocannabinol. Six groups of Ss received discrimination training between a 555 nm stimulus correlated with a variable interval (one minute schedule of reinforcement and a 538 nm stimulus correlated with extinction). Following mastery of the discrimination, each S was tested for generalization, along with wavelength dimension, on two occasions. One test followed the intramuscular injection of isotonic saline, while the other test followed administration of dextro-amphetamine monophosphate at a dose level of 0.00, 0.25, 0.50, 1.00, 2.00, or 3.00mg/kg. Half of the Ss received the drug test first, followed by the saline test. The order was reversed for the other half. Results indicated that the amphetamine compound had no effect on the peak shift or area shift. While the drug reliably steepened the gradient around the 555 nm stimulus, the steepening effect was not dose dependent, suggesting that the effect was due to generalization decrement. (Journal abstract modified)

213275 Gliner, Jeffrey A.; Horvath Steven M.; Wolfe, Robert R. Institute of Environmental Stress, University of California, Santa Barbara, CA 93106 **Operant conditioning of heart rate in curarized rats: hemodynamic changes.** American Journal of Physiology. 228(3):870-874, 1975.

In three groups of curarized rats subjected to operant heartrate conditioning with use of a shock avoidance procedure, cardiac output, mean arterial pressure, and total peripheral resistance were measured. Heartrate changes in the control group remained constant during the entire 90 min experimental period, while cardiac output decreased significantly. Those rats that were reinforced for increasing their heartrate had a small but statistically significant increase in heartrate, but cardiac output decreased to approximately the same extent as in the control group. The group reinforced for decreasing their heartrate demonstrated a large, significant decrease in heartrate and an even larger drop in cardiac output, which was significantly greater than that of either of the other two groups. Operant conditioning of a single facet of the cardiovascular system resulted in significantly larger changes in other cardiovascular parameters, which may have been partly masked by the physiological effects of d-tubocurarine. It is concluded

that only when these other measures of cardiovascular function are taken into consideration can interpretation of operant heartrate conditioning become meaningful. 16 references. (Author abstract)

213350 Yokel, Robert A.; Wise, Ray A. Dept. of Psychology, Center for Research on Drug Dependence, Sir George Williams Univ., Montreal, Quebec H3G 1M8 **Increased level pressing for amphetamine after pimozide in rats: implications for a dopamine theory of reward.** Science. 187(417):547-549, 1975.

The effects of catecholamine blocking agents on lever pressing for intravenous amphetamine reward were assessed in rats. Increased rates of amphetamine self-administration (followed by extinction when high doses are used) is seen after treatment with the doapmine blocking agent pimozide, whereas decreased rates are seen with alpha-adrenergic and beta-adrenergic blocking agents phentolamine and l-propranolol. The effects of low and high doses of pimozide on level pressing resemble the effects of reward reduction and reward termination, respectively; norepinephrine blockade has no such effects. A role in the central mediation of reward perception is suggested for dopamine but not for norepinephrine. 19 references. (Author abstract modified)

05 TOXICOLOGY AND SIDE EFFECTS

206783 Fanelli, O.; Mazzoncini, V.; Ferri, S. SIGMA-TAU S.p.A., Research Dept., I-00040 Pomezia, Rome, Italy **Toxicological and teratological study of 2-phenyl-5,5-dimethyl-tetrahydro-1,4-oxazine hydrochloride (G 130), a psychostimulant drug.** Arzneimittel-Forschung (Aulendorf). 24(10):1627-1632, 1974.

A toxicological study of 2-phenyl-5,5-dimethyl-tetrahydro-1,4-oxazine hydrochloride (G-130), a psychostimulatn drug, was designed to investigate tolerability. G-130 was administered for 180 days at different dose levels in rats and dogs, and only at highest dose levels were toxic effects found. Liver, kidneys, adrenals and thyroid were particularly affected in both animals. The plasma enzymes were also increased. A teratogenic activity study in rats and rabbits showed that G-130 does not induce malformation of fetuses. At highest dose levels some ossification centers were found in the jawbone and the breastbone. In rabbits an increase of reabsorptions and a decrease of mean bodyweight of fetuses appeared. It is concluded that G-130, orally administered, possesses a satisfactory tolerability in rats and dogs. 3 references. (Author abstract modified)

206970 Kreiskott, H. Neuropharmakologische Abteilung, Knoll AG, 67 Lundwigshafen/Rhein, Germany **/Longitudinal profiles of the effects of psychotropic drugs: results of an animal study./** Einfuhrung zum Thema Langsschnittprofile von Psychopharmakawirkungen: Tierexperimentelle Befunde. Arzneimittel-Forschung (Aulendorf). 24(7):974-976, 1974.

The value of studying the longitudinal effects of psychotropic drugs is discussed in view of the long-term therapeutic application of these agents. It is noted that repeated administration, as compared to single dose administration, may lead to alterations in the pharmacological activity profile of psychotropic drugs which appear quantitatively as an increase or decrease and qualitatively as a reversal of the effect, occurrence of side-effects or increased pathological susceptibility, due to immunological reactions. These principles are applied to reports of experiments on effects of neuroleptics, tranquilizers, morphine and barbiturates. The value of longitudinal profiles following single dose administration of long-acting drugs is stressed, and the occurrence of unusual long-term effects (ghost responses) with psychotropic drugs is mentioned. 36 references. (Author abstract modified)

210750 Ho, A. K. S.; Tsai, C. S. Laboratory of Neurochemistry and Neuropharmacology, Wayne State University, College of Pharmacy and Allied Health, Detroit, MI 48202 **Lithium and ethanol preference.** Journal of Pharmacy and Pharmacology (London). 27(1):58-60, 1975.

Evidence is presented that treatment with a dose of lithium comparable to that used in man reduced significantly the volitional consumption of ethanol in rats. In addition, the concentrations of brain acetylcholine showed good correlation with the behavioral observations. The interference in central cholingeric activity by lithium may influence the consumption of ethanol. Other possible actions include the displacement of sodium ions from parts of the brain by lithium ions which may influence the osmoreceptors leading to a shift in water balance. Lithium also influences the metabolism of monoamines, while ethanol preference in animals can be attributed to tryptaminergic activities in the brain. 11 references.

210833 Christensen, Sten. Department of Pharmacology, University of Copenhagen, 20 Juliane Mariesvej, DK-2100 Copenhagen, Denmark **Effects of water deprivation in rats with polydipsia and polyuria due to long-term administration of lithium.** Acta Pharmacologica et Toxicologica (Kobenhavn). 35(3):201-211, 1975.

Wistar with lithium (Li) induced polydipsia and polyuria (group 3) were deprived of water in order to examine their maximal urinary concentrating ability. For comparison, water deprivation was also achieved in rats with polydipsia induced by replacing the drinking water with 5% glucose (group 1) and in rats with hereditary hypothalamic diabetes insipidus (group 2). The animals were totally deprived of water either for 72 hours or until 20% loss of body weight had been obtained. During water deprivation, the urine flow was diminished more rapidly and to a lower level in group 1 than in groups 2 and 3. The results indicate that rats with Li induced polydipsia and polyuria exhibit marked impairment of the renal concentrating ability. 24 references. (Author abstract modified)

210867 Cheng, H. C.; Long, J. P.; Nichols, D. E.; Barfkencht, C. F. Dept. of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52242 **Effects of para-methoxyamphetamine (PMA) on the cardiovascular system of the dog.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 212(1):83-88, 1974.

Para-methoxyamphetamine (PMA) was tested on the cardiovascular system of the dog. PMA caused a long lasting stimulatory effect on arterial blood pressure, heartrate, cardiac output and myocardial contracility. Like tyramine, cardiovascular effects of PMA were antagonized by guanethidine. The increases in heartrate and myocardial contractile force induced by PMA were also blocked by propranolol. It is concluded that PMA causes stimulation of beta-adrenergic receptors of the heart by releasing neurotransmitter from sympathetic nerve terminals. 4 references. (Author abstract)

210868 Antonaccio, M. J.; Robson, R. D. Pharmacueticals Division, Ciba-Geigy Corporation, Summit, NJ 07901 **L-dopa hypotension in dogs: evidence for mediation through 5-HT release.** Archives Internationales de Pharmacodynamine et de Therapie (Ghent). 212(1):89-102, 1974.

The centrally mediated hypotensive and bradycardic effects of Ladopa were investigated in the dog before and after pretreatment with various autonomic antagonists. Pretreatment with haloperidol or chlorpromazine did not prevent the hypotension caused by L-dopa in monoamine oxidase inhibited dogs. Yohimbine did not block apomorphine hypotension but totally prevented or reversed established L-dopa hypotension and bradycardia. Methysergide pretreatment significantly decreased L-dopa-induced hypotension and bradycardia. Pretreatment of dogs with p-chlorophenylalanine (PCPA) signficiantly decreased hypothalamic and cortical but not medullary or thalamic levels of 5-hydroxytryptamine (5-HT). Norepinephrine levels were unaffected. The hypotensive and bradycardic effects of L-dopa were significantly attenuated in the PCPA treated dogs. Reserpine pretreatment abolished L-dopa but not 5-hydroxytryptophan (5-HT) centrally mediated hypotension. The close similarity of the hypothensive and bradycardic actions of 5-HTP and L-dopa and the ability of 5-HT blockers or deplectors to attenuate the L-dopa effects suggest that the centrally mediated hypotensive effects of L-dopa are mediated through central 5-HT release. 28 references. (Author abstract)

210873 Kaymakcalan, Sukru; Sivil, Semuel. Department of Pharmacology, Ankara University Medical School, Sihhiye, Ankara, Turkey **Lack of tolerance to the bradycardic effect of delta9-trans-tetrahydrocannabinol in rats.** Pharmacology (Basel). 12(4-5):290-295, 1975.

Acute and chronic effects of delta9-tetrahydrocannabinol (THC) on the heartrate were studied in unanesthetized rats. THC produced a negative chronotropic effect. Contrary to the many other effects of THC, tolerance did not develop to the bradycardic effect after 16 days of administration. The possible mechanisms of the chronotropic effect of THC are discussed. 25 references. (Author abstract)

210920 Ladefoged, O. Department of Pharmacology and Toxicology, Royal Veterinary College, Bulowsvej 13, 1870 Copenhagen V, Denmark **The effect of LSD, psilocybin, harmaline and amphetamine on the body temperature of parachlorphenylalanine pretreated rabbits.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 208(2):251-254, 1974.

The effects of four psychopharmacologically active compounds on the rectal temperature were examined in both untreated and parachlorophenylalanine (pCPA) pretreated rabbits. Amphetamine, harmaline, lysergic acid diethylamide (LSD) and psilocybin caused hyperthermia in the rabbits. pCPA-pretreatment antagonized the effect of amphetamine and harmaline but potentiated the effects of LSD and psilocybin. 6 references. (Author abstract)

211015 Bright, Thomas P.; Farber, Mark O.; Brown, Daniel J.; Forney, Robert B. Pulmonary Research Laboratories, VA Hospital, Indianapolis, IN 46202 **Cardiopulmonary toxicity of delta9-tetrahydrocannabinol in the anesthetized dog.** Toxicology and Applied Pharmacology. 31(1):100-106, 1975.

Cardiopulmonary toxicity of delta9-tetrahydrocannabinol (THC) in the anesthetized dog was examined. Blood specimens were examined periodically for pO2, pCO2, pH, and lactate and pyruvate concentrations. In addition, cardiac output, heart rate, and lung compliance (CL) and resistance (RL) were measured. THC markedly increased RL in intact dogs but not in vagotomized dogs, while CL remained essentially unchanged in both intact and vagotomized animals. The administration of THC had no effect on arterial blood gases in intact or vagotomized dogs as compared to controls. Intact animals, unlike those vagotomized, exhibited a significant decrease in blood pH. Bradycardia developed in intact animals, which could not be completely prevented by vagotomy. Cardiac output also decreased in intact and, to a lesser extent, in vagotomized animals. Diminished cardiac output was associated with metabolic acidosis characterized by an increase in blood lactate and in the lactate - pyruvate ratio. 16 references. (Author abstract modified)

211494 Harvey, John A.; McMaster, Scott E.; Yunger, Libby M. Dept. of Psychology, University of Iowa, Iowa City, IA 52242 **p-Chloroamphetamine: selective neurotoxic action in brain.** Science. 187(4179):841-843, 1975.

Injection of 2.5, 5, 10, or 20 milligrams of p-chloroamphetamine per kilogram of bodyweight into rats produced evidence of cytopathological changes in sections of brain stained by a Nissl or silver method. As early as 1 day after drug injection, cells demonstrated an intense Nissl staining, intense argyrophilia, cellular shrinkage, and perineuronal spaces. At 30 days after injection both stains revealed cellular debris and glial reactions characteristic of cellular dissolution. The neurotoxic effects of 2.5, 5, or 10 milligrams of p-chloroamphetamine per kilogram were primarily restricted to an area of the ventral midbrain tegmentum corresponding to the distribution of the B-9 serotonergic cell group. After 20 milligrams of p-chloroamphetamine per kilogram there was also evidence of neurotoxic effects on cells within the substantia nigra. These results confirm previous suggestions that the long-term reduction in serotonin content of brain, tryptophan-5-hydroxylase activity, and uptake of serotonin after injection of p-chloroamphetamine is due to a neurotoxic effect of the drug or some metabolite on serotonergic cell bodies. 14 references. (Author abstract)

06 METHODS DEVELOPMENT

206807 Windorfer, A., Jr.; Rottger, H. J. Universitats-Kinderklinik, 78 Freiburg i. Br., Mathildenstrasse 1, Germany **/Micromethods for quantitative determination of sedatives and antipyretics by thermo-gas chromatography./** Mikromethode zur quantitativen Bestimmung von Sedativa und Antipyretika (Aminophenazon, Diphenylhydantoin, Paracetamol, Phenobarbital, Primidon) mit der Thermo-Gas-Chromatographie. Arzneimittel-Forschung (Aulendorf). 24(6):893-895, 1974.

Using a gas chromatographic method, it was possible to analyze and quantitatively assay five therapeutically important drugs: aminophenazone, diphenylhydantoin, paracetamol, phenobarbitone and primidone. For each analysis in duplicate or triplicate, 0.5ml serum are needed. The precision (reproducibility) was in the order of 2 to 3%, the accuracy in the order of 4 to 7%. The limit of detection varied between 0.5micrograms/ml for diphenylhydantoin, 0.8micrograms/ml for phenobarbitone and 1 microgram/ml for aminophenazone and paracetamol. 15 references. (Author abstract modified)

206998 Stille, G. 497 Bad Oeynhausen, Brandenburger Strass 25a, Germany **/Influence of neuroleptic substance on neurophysiological parameters in experimental animals./** Einfluss psychotroper Substanzen auf neurophysiologische Parameter bei Versuchstieren. Arzneimittel-Forschung (Aulendorf). 24(7):1051-1057, 1974.

A neurophysiological approach to the classification of drugs is presented. In general, the first step was to determine the effect of the drug on the normal electroencephalograph of various animal species. The value of computer analysis, such as

autocorrelation, cross correlation and power spectrum, is discussed. For further investigations, use of the various brain systems (functional components of the brain) as a starting point is suggested. These systems include the ascending reticular system, the limbic system and the striothalacortical system. 28 references. (Author abstract modified)

207289 Cattabeni, F.; Racagni, G.; Paoletti, R. Institute of Pharmacology and Pharmacognosy, University of Milan, 20129 Milan, Italy **A mass fragmentographic study of amphetamine and metabolites in rat brain.** Journal of Psychiatric Research (Oxford). 11:45-51, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, mass fragmentography utilized for the investigation of amphetamine (A) hydroxylated metabolites and analogues in rat brain was reported. This method makes a careful determination of A metabolites in different brain areas and the subcellular fraction possible. Correlations between the formation and accumulation of single metabolites and the behavioral and metabolic effects of A and analogues are discussed. The mass fragmentographic procedure is also applied to the study of A metabolites and analogues in the cerebrospinal fluid of patients with A intoxication and schizophrenia. 32 references. (Author abstract)

207549 Tobler, H. J.; Regez, J. L.; Walliser, C. Basic Medical Research Dept., Sandoz Ltd., Basel, Switzerland **The electroencephalogram as a physiological and pharmacological observable.** Triangle (Basel). 12(4):177-181, 1973.

The use of the electroencephalograph (EEG) as a tool for basic and applied physiological and pharmacological research is discussed, and advantages of using this technique for investigation and classification of the effects of substances acting on the central nervous system (CNS) are reviewed. Spectrum analysis is used to quantify the EEG for correlation with other physiological variables. Laboratory findings are summarized which indicate that the quantified EEG is a valid physiological observable which is suitable for the assessment of metabolic and neuronal activity as well as the whole functional state of the CNS. The emphasis in these investigations is the study of cerebral insufficiency by means of the administration of ergot alkaloids to animal models. 25 references.

210786 Gerber, H. R.; Anton, A. H. Department of Anesthesiology, Case Western Reserve University, School of Medicine, Cleveland, OH 44106 **A bacterial model for the evaluation of barbiturates.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 212(2):284-296, 1974.

Using cultures of Eschericia coli as a biological model, several correlations were obtained between the antibacterial activity of several diverse barbiturates, certain of their physicochemical characteristics and their biological activity in man. Only biologically active barbiturates, whether hypnotics or convulsants, had antibacterial activity. Antibacterial activity was associated with the unionized moiety of the barbiturates. Compounds with a negligible chloroform to water coefficient, i.e.,poor lipid solubility, had no antibacterial activity. Barbiturate inhibition was readily reversed by washing the culture with saline. Sulfur and oxygen analogs were equipotent in this system. 23 references. (Author abstract)

210885 Cheney, D. L.; Costa, E.; Hanin, I.; Trabucchi, M.; Wang, C. T. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Application of principles of steady-state kinetics to the in vivo estimation of acetylcholine turnover rate in mouse brain.** Journal of Pharmacology and Experimental Therapeutics. 192(2):288-296, 1975.

The rate of metabolism of acetylcholine (ACh) in mouse brain in vivo was estimated utilizng a radio gas chromatographic approach and pulse labeling with radioactive phosphorylcholine. A kinetic model describing the change with time of the plasma choline (Ch), brain Ch and ACh specific radioactivities as interdependent variables is postulated. ACh turnover rate in mouse brain has been calculated to be 0.36 micromol/g/hr with the least mean squares method, whereas the finite difference method yields slightly lower values. Because of the compartmentalization of brain Ch and the inherent assumptions, the new method can be used only for data collected during the exponential decline of plasma radioactive choline. 14 references. (Author abstract modified)

211007 Maulding, H. V.; Polesuk, J.; Rosenbaum, D. Pharmacy and Analytical Research Department, Sandoz-Wander, Inc., East Hanover, NJ 07936 **Practical kinetics I; quantitation of barbiturate stability by TLC.** Journal of Pharmaceutical Sciences. 64(2):272-274, 1975.

The application of established techniques to the quantitation of stability investigations of liquid formulations as well as in solution kinetic studies is described. The process consists of streaking aliquots of reaction solution on TLC plates, development, elution, and analysis of the substances in the eluate. Several barbiturates were investigated regarding their decomposition at elevated temperatures. Reasonable correlation is noted between obtained rate constants and literature data. This technique represents a utilitarian approach to stability screening of compounds in solution, aqueous or otherwise, where chromatographic separation and analytical methodology for the pure compound are available. 11 references. (Author abstract)

211008 Maulding, H. V.; Nazareno, J. P.; Pearson, J. E.; Michaelis, A. F. Pharmacy and Analytical Research Department, Sandoz-Wander, Inc., East Hanover, NJ 07936 **Practical kinetics III: benzodiazepine hydrolysis.** Journal of the Pharmaceutical Sciences. 64(2):278-284, 1975.

The velocity constants for chlordiazepoxide hydrolysis were measured by independent techniques. A quantitative thin layer chromatography kinetic procedure is compared with an extractive method. The data derived from both processes are in approximate agreement, further exemplifying the feasibility of TLC for rapid stability evaluation of liquid formulations as well as solution kinetic studies. In the extractive procedure, benzodiazepine substrate was separated from the lactam product by methylene chloride extraction of acidic aqueous solution. The TLC procedure consisted of separation on silica gel plates followed by elution and subsequent analysis. The log k-pH relationship for the hydrolysis representing water addition coupled with expulsion of methylamine is presented. Both general acid catalysis and general base catalysis were evidenced, with borate, acetate, formate, and phosphate buffers accelerating the conversion of chlordiazepoxide to lactam. At pH values below neutrality, nonlinear dependency of the rate constant on buffer concentration was observed. This finding may be explained by a change in the rate determining step as buffer concentration varied. 17 references. (Author abstract modified)

211010 Turner, Carlton E.; Henry, Janis T. Research Institute of Pharmaceutical Sciences, School of Pharmacy, Univ. of Mississippi, University, MS 38677 **Constituents of Cannabis sativa L. IX: stability of synthetic and naturally occurring can-**

nabinoids in chloroform. Journal of Pharmaceutical Sciences. 64(2):357-359, 1975.

Additional data indicating the choice of chloroform as solvent for synthetic and naturally occurring cannabinoids are reported. The basic procedure for chloroform extraction of cannabinoids is outlined and the results of a 3 month stability study for a large number of cannabinoids are summarized. The stability of the various compounds was verified using gas - liquid chromatography. While unusual stability problems were observed with different batches of chloroform, individual synthetic cannabinoids and a mixture of synthetic cannabinoids are stable in chloroform and do not decompose. 9 references.

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

206805 Bente, D.; Koeller, D. M.; Koufen, H.; Pietzcker, A.; Schulte, P. W. Psychiatrische Klinik II der Freien Universitat Berlin, 1 Berlin 19, Nussbaumallee 36, Germany /**Clinico-statistical study of the effects of sulpiride, a new neuroleptic drug.**/ Klinisch-statistische Untersuchung des Wirkungsbildes von Sulpirid, einem neuen Psychopharmakon. Arzneimittel-Forschung (Aulendorf). 24(1):107-111, 1974.

Psychopathological and other clinical data on 44 psychiatric inpatients who were treated with sulpiride for a 30 day period are presented. Statistical analysis of findings indicates that sulpiride is a neuroleptic drug with a large scale of therapeutic effects and a low rate of side-effects. The influence of the drug on the target symptoms of a diagnostically heterogenous group of patients was not very intensive and was seen only after a longer period of application. Sleep disturbances, overstimulation and agitation were observed in some cases. 7 references. (Author abstract modified)

207311 Goodwin, Frederick K.; Sack, Robert L. Section on Psychiatry, Laboratory of Clinical Science, N.I.M.H., Bethesda, MD 20014 **Behavioral effects of a new dopamine-beta-hydroxylase inhibitor (fusaric acid) in man.** Journal of Psychiatric Research (Oxford). 11:211-217, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, results of a clinical trial of fusaric acid (a dopamine-beta-hydroxylase (DBH) inhibitor) in patients with primary affective disorders (mania and depression) were reported. Fusaric acid was well tolerated with a minimal effect on blood pressure and no alteration in indices of hepatic, hematologic, renal or endocrine function. Chronic administration of fusaric acid caused changes in central amine metabolism which are predicted from its reported mechanisms of action. Conventional antimanic therapies (lithium, phenothiazines) initiated after the fusaric acid protocol were associated with improvement in the expected time period in all the patients. The data on the behavioral effects of a DBH inhibitor in manic-depressive patients may have some bearing on the role of catecholamines in schizophrenia. 34 references.

209787 Noyes, Russell, Jr.; Brunk, S. Fred; Baram, David A.; Canter, Arthur. Dept. of Psychiatry, University of Iowa College of Medicine, Iowa City, IA 52242 **Analgesic effect of delta-9-tetrahydrocannabinol.** Journal of Clinical Pharmacology. 15(2-3):139-143, 1975.

A preliminary trial of oral delta9-tetrahydrocannabinol (THC) is reported which demonstrated an analgesic effect of the drug in patients experiencing cancer pain. Placebo and 5mg, 10mg, 15mg and 20mg THC were administered double-blind to 10 patients. Pain relief significantly superior to placebo was demonstrated at the 15mg and 20mg level. At these levels, substantial sedation and mental clouding were reported. 12 references. (Author abstract modified)

209791 Harris, Martin. Dept. of Psychiatry, Health Sciences Division, Virginia Commonwealth University, Richmond, VA **Treatment of acute schizophrenia with a new butyrophenone -- Lenperone.** Journal of Clinical Pharmacology. 15(2-3):187-190, 1975.

The efficacy and safety of lenperone, a new butyrophenone, were examined in a 4 week, open study of seven acute schizophrenic inpatients. The Brief Psychiatric Ratings Scale, Nurse's Observation Scale for Inpatient Evaluation, Clinical Global Impression Scale and Treatment Emergent Symptoms Scale were used to assess clinical results. The drug appeared to have definite antipsychotic activity at an optimal dosage of 85mg to 112mg daily. There was a decrease in the degree of bizarre ideation, concept disorganization, affective blunting, delusions, hallucinations and agitation. Anxiety was lessened but depression appeared unaffected. Side-affects were similar to those of other antipsychotic agents, and all patients showed electrocardiographic changes. Sedation was moderate, and extrapyramidal symptoms were presented in one and probably two patients; autonomic side-effects were mild. Significant orthostatic hypotension occurred in one patient. 3 references. (Author abstract modified)

08 DRUG TRIALS IN SCHIZOPHRENIA

205613 Molcan, J.; Novotny, V.; Schlupkova, L. Psychiatric Clinic, Mickiewiczova 13, 801 00 Bratislava, Czechoslovakia **Our experience with clozapine treatment.** Activitas Nervosa Superior (Praha). 16(3):200-201, 1974.

At the 16th Annual Psychopharmacological Meeting, a study of clozapine given to 20 psychotics was reported. The therapeutic effect of the drug was better in acute cases where it influenced in the first place disintegration of thought, delusion of persecution, bizarre thought contents and attitude to reality, and in the second place hallucinations, weakening of dynamogenesis and reduced emotionality which corresponded with clinical observations. In the group of chronic schizophrenics improvement was most marked in emotional contact. In chronic schizophrenia the psychotolytic effect set in later than the inhibitory and anxiolytic effect and this was more pronounced than in the acute cases, perhaps as a result of a greater resistance of the basic symptoms. Most frequent side-effects were somnolence, subfebrile and febrile states, tachycardia, hypokinesia and dyskinesia, dizziness, sleep disturbance, hypersalivation, and perspiration.

205617 Preiningerova, O.; Hanus, H.; Zapletalek, M. Psychiatric Clinic, Hradec Kralove, Czechoslovakia **Clozapine in outpatient practice.** Activitas Nervosa Superior (Praha). 16(3):204-205, 1974.

At the 16th Annual Psychopharmacological Meeting, a study of the use of clozapine in an outpatient practice was reported. A longterm observation of the electroencephalograph (EEG) showed in three patients persisting slight general changes in the record in the course of 4-10 months. Of 20 patients in whom the EEG was repeatedly examined, slight general changes in the record were found in 15 patients. In one young schizophrenic synchronous episodes of theta and delta waves of higher amplitude, with occasional sharper peaks, occurred after the introduction of clozapine. The finding became normal a fortnight after drug withdrawal, reappeared again after the administration of the drug and disappeared after its discontinuation. 3 references.

205618 Faltus, F. Psychiatric Clinic, Praha 2, Ke Karloha 11, Czechoslovakia **Clozapine in the maintenance therapy of schizophrenia.** Activitas Nervosa Superior (Praha). 16(3):205-206, 1974.

At the 16th Annual Psychopharmacological Meeting, a study of the use of clozapine (Leponex) in the maintenance therapy of schizophrenia was presented. If during the initial period of 30-40 days of Leponex treatment the chief psychotic symptoms receded distinctly, then further treatment was regarded as maintenance therapy and dosage was reduced. In four patients of the sample the illness was exacerbated during treatment, in one of these twice. All these exacerbations could be managed with increased Leponex doses. Twice these patients had to be hospitalized. The best improvement was achieved with Leponex and IMAP. The advantage of Leponex is in the fact that an acute exacerbation can be controlled by increasing its dose. At doses which ranged mostly between 50-200mg the patients were troubled primarily by fatigue and an increase in weight. In no case was treatment interrupted because of undesirable side-effects.

206044 Hirsch, Steven R. Department of Psychological Medicine, Westminster Medical School, Queen Mary's Hospital, Roehampton, SW15 5PN, England **The management of schizophrenia outside the hospital: research findings and underlying principles.** Indian Journal of Psychiatry (Madurai). 16(2):145-158, 1974.

Research findings from the Medical Research Council Social Psychiatry Unit which directly bear on the management of schizophrenia are reviewed. Radical changes in the approach to treatment in Great Britain, which have led to a marked reduction in the length of hospital stay and the number of psychiatric beds, are considered. A theory of disability and handicap, which relate to the patient's symptoms and the effect of different forms of management is put forth with the scientific evidence which supports it. The interaction between environmental factors which precipitate acute symptoms and psychoactive drugs which raise the patient's threshold of susceptibility to those influences is discussed in the light of recent controlled drug trials. An approach to management which is low in cost, can be administered in urban health centers using phenothiazines and accounts for the special conditions of developing countries is suggested. 32 references. (Author abstract modified)

206332 Cho, H. W.; Meltzer, H. Y. Dept. of Psychiatry, Univ. of Chicago Pritzker School of Medicine, Chicago, IL **Mg++-dependent adenosine triphosphatase activity in erythrocyte ghosts of schizophrenic patients.** Biological Psychiatry. 9(2):109-116, 1974.

"Membrane" adenosine triphosphatase (ATPase) activity, which was predominantly Mg++ dependent ATPase activity, was determined in erythrocyte ghosts from nine unmedicated schizophrenic patients and controls. Seven of nine acute and chronic schizophrenic patients had greater membrane red cell ghost ATPase activity than their paired controls. The membrane ATPase activity of both patients and controls was inhibited by ouabain, which differs from patients with various types of muscular dystrophy who have been found in some studies to have increased erythrocyte ghost membrane ATPase activity in the presence of ouabain. Chlorpromazine treatment did not diminish the erythrocyte membrane ATPase activity of two schizophrenic patients. Elevated activity of Mg++ ATPase in neuronal tissues might affect their excitability and thus have considerable significance for the etiology of psychotic states. 28 references. (Author abstract)

206337 Doust, John W. Lovett. Section of Psychophysiology, Clarke Insitute of Psychiatry, Toronto, Ontario, Canada **Cerebral hemodynamic effects of chronic tryptophan feeding in man as measured by quantified cerebal impedance plethysmography.** Biological Psychiatry. 9(2):171-180, 1974.

Heavy L-tryptophan was administered to a group of schizophrenic patients and aspects of cerebral circulation were measured concurrently by an electrical impedance technique. Since it has been amply confirmed in animals that tryptophan feeding leads to an increase in brain serotonin, it may be assumed that in man a similar increase in this neurotransmitter would occur in the 3 weeks that this amino acid was given. Aspects of the cerebral circulation of seven female schizophrenics were monitored daily for 3 weeks to obtain a baseline determination, then for a second 3 week treatment with phenelzine (a monoamine oxidase inhibitor), and then for weeks of phenelzine lpus L-tryptophan. Measurements were made by a method of quantified cerebral impedance plethysmography. Results show a significant increase in the electrical analog of carotid blood flow in five of the seven patients following tryptophan feeding. Inconstant changes in indices of cerebral blood flow and cerebrovascular resistance were also observed. No significant changes were seen in arterial pressure or in pulse rate. 31 references. (Author abstract modified)

206603 Ban, Thomas A. Division of Psychopharmacology, McGill University, Montreal, Canada **Pharmacotherapy of schizophrenia: facts, speculations, hypotheses and theories.** Psychosomatics. 15(4):178-187, 1974.

The introduction of chlorpromazine and the development of other neuroleptic drugs used in treating schizophrenia has ameliorated schizophrenic symptoms and allowed some patients to participate in the community and enter into marriages. However, these drugs have not cured the disease. Considering the accumulating evidence that schizophrenia is a hereditary genetically determined disease, it seems likely that the population of schizophrenics will increase. The recognition that neuroleptics have a limited effect has resulted in other drug therapies being tested. These include dimethoxyphenylethylamine, adrenochrome, indoleamines, and catecholamines. 100 references.

206784 Fischer-Cornelssen, K.; Ferner, U.; Steiner, H. Medizinisch-Biologische Forschung, Sandoz AG, CH-4002, Basel, Switzerland **/Multifocal trial of psychotropic drugs ("multihospital trial")./** Multifokale Psychopharmakaprufung ("Multihospital Trial"). Arzneimittel-Forschung (Aulendorf). 24(10):1706-1724, 1974.

A multifocal approach to the design and analysis of double-blind studies is described and results of a trial using clozapine (LX) and chlorpromazine (CH) are reported. Base data on dosage, therapeutic effect, and both subjective and objective side-effects were collected in a uniform manner, and findings relating to 1000 data items on 217 patients were processed by computer. Results testify to the therapeutic superiority of LX over CH in acute, relapsing and exacerbating schizophrenia of the paranoid hallucinatory and catatonic type. With an average dosage of 300mg daily, LX was marked by more effective than CH, particularly in the more serious cases. Statistically significant evidence was found for the four stage action of LX. Results demonstrate the value of a rational, broadly based, balanced and multifocal approach to the recording and evaluation of data from drug trials. 7 references. (Author abstract modified)

206933 Mielke, D. H.; Gallant, D. M.; Oelsner, T.; Kessler, C. M.; Tomlinson, W. K.; Cohen, G. H. Tulane University School of Medicine, New Orleans, LA **Butaclamol**

hydrochloride (AY-23,028): an early evaluation in severely ill schizophrenics. Diseases of the Nervous System. 36(1):7-8, 1975.

The efficacy and safety of butaclamol hydrochloride (AY-23,028), a new type of compound having the benzocycloheptapyridisoquinolinel ring structure, was evaluated in 12 severely ill schizophrenic patients. Findings from exploratory uncontrolled clinical trials indicate that the drug is an active antipsychotic agent, with beneficial behavior changes appearing at 20mg/day dosage. Global ratings of clinical change were made independently by two psychiatrists and two research nurses at the time of baseline, midway, and final evaluations, and ratings showed a high level of agreement. Findings obtained from the rating scales strongly support the clinical global ratings. Several extrapyramidal symptoms were noted as side-effects. 3 references.

206975 Gross, H.; Langner, E.; Pfolz, H. Psychiatrisches Krankenhaus der Stadt Wien, Baumgartnerhohe 1, A-1145 Vienna, Austria **/Clozapine in long-term therapy of chronic schizophrenia./** Clozapin in der Langzeittherapie der chronischen Schizophrenie. Arzneimittel-Forschung (Aulendorf). 24(7):987-989, 1974.

Clozapine, a major tranquilizer, was studied in chronic schizophrenics and found to be efficient in long-term therapy for psychoses with foremost productive symptoms. The restriction of the awake consciousness (in about 40% of the cases) was controlled by combining clozapine with a major tranquilizer of smaller therapeutic range. Such combinations were also useful if productive symptoms were not suppressed sufficiently. It is suggested that patients inclining to autonomic instability not be treated with clozapine. The lack of extrapyramidal side-effects of clozapine is cited as a distinct advantage over other major tranquilizers. 8 references. (Author abstract modified)

206978 Eckmann, Friedrich. 2380 Schleswig, Fachkrankenhaus fur Psychiatrie and Neurologie, Germany **/Clinical study on sulpiride in long-term hospitalized schizophrenic patients./** Klinische Untersuchungen mit Sulpirid bein langjahrig hospitalisierten schizophrenen Kranken. Arzneimittel-Forschung (Aulendorf). 24(7):993-994, 1974.

In a clinical study of sulpiride treatment of schizophrenia, sulpiride was administered to 112 male patients who had been hospitalized for many years. The drug was given for 3 weeks in daily doses of 600mg in an open trial. Sulpiride was shown to produce more favorable effects on hebephrenic schizophrenia than paranoid and catatonic types. Patients with unproductive schizophrenia benefited more than those suffering from productive types. Statistical evaluation of the results in terms of three psychopathological characteristics (hallucinations and/or delusional ideas, agitation, autism and their combinations) revealed that autism responded most favorably to the drug. 4 references. (Author abstract modified)

206983 Fischer-Cornelssen, K.; Ferner, U.; Steiner, H. Medizinisch-Biologische Forschung, Sandoz AG, CH-4002, Basel, Switzerland **/Multispectral investigation of psychotropic drugs./** Multifokale Psychopharmakaprufung. Arzneimittel-Forschung (Aulendorf). 24(7):1006-1007, 1974.

A multihospital clinical trial of clozapine is used to illustrate the value of a multifocal approach to the investigation and analysis of drug trials. This method utilizes 1000 items of data per patient in a computerized process to evaluate and weigh therapeutic effects and subjective and objective side-effects. Clozapine was compared with chlorpromazine (CH) in a stringent double-blind study, and every effort was made to achieve uniformity regarding starting conditions, conducting and evaluating trials, trial protocol and patient data sheets. Results testify to the therapeutic superiority of clozapine over CH in acute, relapsing and exacerbating schizophrenia of the paranoid hallucinatory and catatonic types and indicate the value of a rational, broadly based, balanced and multifocal approach to recording and evaluating the data. (Author abstract modified)

207292 Gjessing, Leiv R. no address **Catecholamines and antipsychotic drugs in periodic catatonia.** Journal of Psychiatric Research (Oxford). 11:71, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the role of catecholamines and antipsychotic drugs in periodic catatonia, a "schizophrenic" subgroup, was examined. During the spontaneous course of each psychotic phase, stuporous or excited, the urinary excretion of the catecholamines and their methylated and acidic derivatives is increased. In the psychotic phase the vegetative state is predominantly adrenergic with mydriasis, exophtalmos, salivation, pallor, increased pulse rate, and increased blood pressure. By giving reserpine, haloperidol and chlorpromazine, most of the vegetative and the psychotic symptoms are suppressed or abolished, but the patient may remain functioning at the interval level without complete recovery.

207293 Smythies, J. R.; Beaton, J. M. no address **A pilot study of pimozide in schizophrenia.** Journal of Psychiatric Research (Oxford). 11:71-72, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the response of schizophrenics to pimozide was reported for a population of 12 chronic schizophrenic patients given 10 mg/day of pimozide. The three patients who got markedly better were the kind of patients who hardly ever respond to phenothiazines. The patients who got markedly worse, or quite considerably worse, were patients of the normally overactive aggressive, hallucinated, deluded type. Pimozide seems to affect a different population, suggesting that these two different populations of schizophrenics have a different kind of biochemistry; maybe the ones who respond to pimozide have something specifically wrong with their dopamine systems, because we know that pimozide is specifically a dopamine blocker.

207295 Sedvall, Goran; Fyro, Bengt; Nyback, Henrik; Wiesel, Frits-Axel; Wode-Helgodt, Birgitta. Departments of Pharmacology and Psychiatry, St. Goran's Hospital, Karolinska Institutet, Stockholm, Sweden **Mass fragmentometric determination of homovanillic acid in lumbar cerebrospinal fluid of schizophrenic patients during treatment with antipsychotic drugs.** Journal of Psychiatric Research (Oxford). 11:75-80, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the role of antipsychotics and homovanillic acid (HVA) in cerebrospinal fluid was discussed. HVA is the single compound useful for indirect determination of brain dopamine turnover in man. Clinical doses of chlorpromazine, haloperidol and thioridazine elevated the level of HVA in CSF of most schizophrenic patients. Results are compatible with the view that brain dopamine synthesis is accelerated in schizophrenics undergoing treatment with an-

tipsychotic drugs. Results encourage a further analysis of the relationship between the pharmacodynamics effect demonstrated and clinical and pharmacokinetic parameters. 20 references.

207534 Kato, Takashi; Morita, Shonosuke; Ishijima, Hiroshi. Municipal Otaru Seiwa Hospital, Japan **Clinical use of Clocapramine for the treatment of chronic schizophrenia -- special emphasis on its comparison with perphenazine.** Medical Consultation and New Remedies (Tokyo). 11(8):245-249, 1974.

The effect of clocapramine (Cl) on chronic schizophrenics was compared with that of perphenazine (Pe), based on an experiment in which 21 21-61 year old chronic schizophrenic patients with 6-32 years of schizophrenic history were treated with Pe (6-36 mg/day) for at least 3 months, followed by treatment with Cl (45-270 mg/day) for 2 months, and were again treated with Pe (same as above). Cl improved volition and communication slightly more than Pe. No significant difference in the effect was observed among different doses of Cl, however, the maximum daily dose of Cl was considered to be 150 mg. The major side-effect of Cl was insomnia, but no special treatment was required. In order to prevent extrapyramidal syndrome, appropriate antiparkinson agents may be necessary. 4 references.

207643 Kishimoto, Akira; Inagaki, Takashi; Motoike, Mitsuo; Miyamoto, Keiichi; Ogura, Chikara; Oda, Takao. Shimane Prefectural Mental Hospital, Japan **Dose level and effects of trifluperidol in clinical use for schizophrenia.** Clinical Psychiatry (Tokyo). 16(6):586-587, 1974.

The effect of different doses of trifluperidol (TFP) in treating schizophrenia was assessed. Three treatment groups were established, less than 6mg/day, 7-14mg/day, and more than 15mg/day. The treatment was undertaken with or without other psychotropic drugs, antiparkinson agents and hypnotics. All treatment groups showed a remission rate of roughly 30%; the lowest and highest dose levels were most effective. Small and medium doses were most effective in hypoactivity, and small doses were most useful in autism. Dose level did not alter the drug's effect on delusion and hallucination, but large doses produced the strongest effect on communication and psychomotor excitation. The types and occurrence of side-effects are summarized. 9 references.

207788 Coleman, Mary. 2525 Belmont Road, N.W., Washington, DC 20008 **A crossover study of allopurinol administration to a schizophrenic child.** Journal of Autism and Childhood Schizophrenia. 4(3):231-240, 1974.

Metabolic evaluation of an 11-year-old schizophrenic child revealed a slight elevation of uric acid in the urine. A crossover trial of allopurinol (a xanthine oxidase inhibitor) and placebo was completed. Psychiatric symptoms slowly regressed during the allopurinol period and partially returned during the placebo period. The relationship between purine overproduction and psychiatric symptoms is discussed. 19 references. (Author abstract)

208325 Chapman, Loren J.; Cameron, Richard; Cocke, Joseph G.; Pritchett, Thomas. Psychology Department, Charter at Johnson Street, University of Wisconsin, Madison, WI 53706 **Effects of phenothiazine withdrawal on proverb interpretation by chronic schizophrenics.** Journal of Abnormal Psychology. 84(1):24-29, 1975.

Forty two chronic schizophrenics were given a clinical form of the Gorham Proverbs Test while receiving antipsychotic medication and two forms 4 weeks after drug withdrawal. Some patients improved with drug withdrawal and some worsened. Scores of autism in proverb interpretation and ratings of clinical status agreed on which patients improved or worsened. 19 references. (Author abstract modified)

208622 Friemert, Klaus; Beier, Rolf; Vehreschild, Torsten. Universitats-Nervenklinik Rostock, DDR-25 Rostock-Gehlsheim, East Germany /**Results of therapy with Lyogen-Depot in schizophrenic illness.**/ Behandlungsergebnisse mit Lyogen-Depot bei schizophrenen Erkrankungen. Psychiatrie, Neurologie und medizinische Psychologie (Leipzig). 26(6):374-377, 1974.

Twenty three patients with chronic schizophrenia and spasmodic fits and 10 patients who had had a first acute fit were administered 12.5mg Lyogen-Depot i.m. every 3 weeks after the psychotic episode has subsided. A statistically significant decrease in relapses in the patients was found. In one third of the patients a simultaneous administration of antiparkinson drugs was necessary because of extrapyramidal side-effects. Two thirds of the patients felt some fatigue 1 to 3 days after the injection. The therapeutic results were generally favorable, and a wider application of repository neuroleptics for the treatment of chronic schizophrenia is recommended. 11 references. (Journal abstract modified)

208631 Blanc, Marcel. no address /**Drugs, mediators, and schizophrenia.**/ Drogues, mediateurs et schizophrenie. Recherche (Paris). 5(51):1096-1099, 1974.

Models of some of the chemical mediators of nervous transmission in the central nervous system were developed in an investigation of psychic functioning. Dopamine and noradrenaline are identified as catecholamines, serotonin as an indoleamine. Further models of neurophysiological transmission of a synaptic - nervous nature were developed. Certain drugs tested blocked either or both of these transmission patterns in part; others stimulated transmission and still others had analogous molecular structure to receptors, and thus altered the role of the mediator. These models are examined in relation to the "psychedelic" phase of schizophrenia and the effects of actual psychedelic drugs. In the current stage of investigation, it can be concluded only that dopamine is implicated in schizophrenia. 7 references.

208862 Hoffer, John. Canadian Schizophrenia Foundation, 2135 Albert Street, Regina, Saskatchewan, S4P 2V1 Canada **The controversy over orthomolecular therapy.** Journal of Orthomolecular Psychiatry (Regina). 3(3):167-185, 1974.

The American Psychiatric Association's "Task Force Report on Megavitamin and Orthomolecular Therapy in Psychiatry" is reviewed. The report criticizes the research finding that orthomolecular therapy can produce a significant improvement in acute schizophrenics, and it is felt that this criticism is unfounded. It is maintained that experimental results cited as evidence of the ineffectiveness of this type of treatment are based on improper experimental procedures. The conclusions of the report's authors are found to be contradicted by their own words in other studies. The report is judged to be full of scientific error and bias. 2 references.

208981 Bernardini, B. Ospedale Neuropsychiatrico di Volterra, Volterra, Italy /**Clinical trends and psychometric appraisal of a group of schizophrenics treated with thiothixene (Navane).**/ Giudizio clinico e valutazioni psicometriche in un gruppo di schizofrenici trattati con Tiotixene (Navane). Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(5):1016-1034, 1973.

Clinical, psychopharmacological and chemical characteristics of thioxanthene derivatives are examined. Results from the administration of thiothixene to a group of 50 schizophrenics, all inpatients of the Volterra Psychiatric Hospital, are discussed. Clinical judgment and objective rating scales were used to evaluate the results. It is concluded that thiothixene induces uninhibited activity and has a stimulating effect on mood and activity and hallucinatory action. The use of thiothixene is recommended in the treatment of paranoia, schizophrenia and catatonia. 53 references. (Journal abstract modified)

209071 Vallillo, R.; Zubiani, A. Istituto Psichiatrico Provinciale Paolo Pini, Milan, Italy. **/Flupenthixol decanoate in psychotic adults -- pilot study./** Il flupentixol decanoato in psicotici adulti -- ricerca pilota. Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(3):692-702, 1973.

A thioxanthene derivative, Flupenthixol decanoate (KC 5391), was used for treating 24 adult psychotics. The drug dosage was 20mg weekly. The treatment results were evaluated based on a simple clinical judgment and on scores according to the Goodrich QPSS Rating Sheet. Psychotic manifestations were favorably affected in 14 patients. In 6 cases, treatment was ineffective and in 4 cases, morbid symptomatology worsened. It is concluded that Flupenthioxol decanoate is a valid therapeutic agent for chronic schizophrenic psychoses especially in cases where blocking dynamics prevail. 10 references. (Journal abstract modified)

209147 Catalano, A.; Gherardi, G. Istituto Psichiatrico "S. Lazzaro", Reggio Emilia, Italy **/Comparison of neuroleptics in controlled experimental conditions: methophenazine vs perphenaxine./** Confronto di neurolettici in condizioni sperimentali controllate: metofenazato vs perfenazina. Riv. Sper. di Freniatria e. Med. Legale delle Alienazioni Ment. (Reggio). 98(2):366-387, 1974.

The activity of two neuroleptic drugs, methophenazine and perphenazine, were compared by an experimental, controlled "crossover" method with a population of 23 chronic schizophrenic patients. No significant difference was found between the two drugs after administration of the Brief Psychiatric Rating Scale and the Scale of Psychiatric Classification. With respect to the "spectrum of activity", perphenazine seemed more effective with "affective insensibility" and methophenazine with "mannered behaviors". Methophenazine caused milder and rarer side-effects than perphenazine. 21 references (Journal abstract modified)

209394 Kato, Hideaki; Kaitani, Hisanori; Mikami, Yasushi; Tanaka, Minoru. no address **Clinical application of oxypertine -- its characteristics as a strong tranquilizer.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(1):107-115, 1974.

The effect of oxypertine on schizophrenia was studied in 27 chronic schizophrenics treated with the drug for a 10 week period. The drug was somewhat effective in less than half of the sample. The drug improved interpersonal relationships, awareness of mental illness, language, and attitude. It is concludeed that the drug is effective in improving human relationships. 16 references.

209402 Itakura, Saburo. no address **Dosage of a psychotropic drug to prevent relapse in a cured schizophrenic patient.** Psychiatria et Neurologia Paediatrica Japonica (Tokyo). 13(2/3/4):171-177, 1973.

Prophylactic administration of sulpiride to prevent schizophrenic relapse is considered based on data from 36 schizophrenic patients in remission. A daily dose of 600mg is considered most appropriate for long-term use. A higher dose produces a manic state indistinguishable from endogenous manic disease, and a lower dose is less effective in the preliminary stages of relapse. 18 references.

209405 Mori, Yashuhiro. no address **Personal experience in the use of sulpiride (FK-880) on schizophrenia.** Medical Consultation and New Remedies (Tokyo). 10(2):365-380, 1973.

The effect of sulpiride in treating schizophrenia was examined in 25 patients treated with sulpiride in combination with promethazine, biperiden, or trihexyphenidyl. The drug showed favorable effects on 70% of the Ss, with effects beginning to appear within 2 weeks after the initiation of treatment. Sulpiride was most effective on hallucination and delusion in newly admitted patients and on chronic patients in a state of acute aggravation, particularly in Ss with catatonic schizophrenia. Side-effects, mostly tremor of fingers and eyelids, was observed in 84% of the sample. 13 references.

209484 van der Velde, Christian D. Kiltie, Harriet. A. Ribicoff Research Center, Norwich Hospital, Norwich, CT 06360 **Effectiveness of loxapine succinate in acute schizophrenia: a comparative study with thiothixene.** Current Therapeutic Research 17(1):1-12, 1975.

Clinical effectiveness of loxapine succinate, a new neuroleptic agent, was compared with the efficacy of thiothixene and placebo during a 6 week double-blind study with 76 patients hospitalized with acute symptoms of schizophrenia. Loxapine appeared to be clearly superior to placebo and significantly superior to thiothixene as well on many items and factors of the Brief Psychiatric Rating Scale and the Nurses' Observation Scale for Inpatient Evaluation. No efficacy measure showed superiority of thiothixene over loxapine. 7 references. (Author abstract)

209701 Cassano, G. B.; Castrogiovanni, P.; Conti, L.; Bonollo, L. Institute of Psychiatry, University of Pisa Medical School, Pisa, Italy **Sulpiride versus haloperidol in schizophrenia: a double-blind comparative trial.** Current Therapeutic Research. 17(2):189-201, 1975.

A multicenter cooperative study of 76 patients with paranoid or hebephrenic schizophrenia who have been treated with sulpirirde or haloperidol in a double-blind trial is reported. Sulpiride was about as active as haloperidol and showed a more rapid onset of therapeutic effects and a wider spectrum of activity. No significant differences were reported for side-effects. Findings also demonstrate the utility and efficiency of using automatic techniques for analysis of data, diagnostic definition of individual patients, and psychopathological profiles characterizing different groups of observations, especially in multicenter trials. 10 references. (Author abstract modified)

209790 Bergling, Roland; Mjorndal, Tom; Oreland, Lars; Rapp, Walter; Wold, Svante. Dept. of Pharmacology, University of Umea, Umea, Sweden **Plasma levels and clinical effects of thioridazine and thiothixene.** Journal of Clinical Pharmacology. 15(2-3):178-186, 1975.

The effects of thioridazine and thiothixene were studied by a double-blind technique in 40 schizophrenic patients. Doses were adjusted for optimal clinical and therapeutic effects, and side-effects were rated after 3 and 8 weeks of treatment. No statistically significant differences were observed between the two drugs or between either of these drugs and the previous

medication. No correlation was found between plasma levels and clinical effects for either thioridazine or thiothixene. Plasma levels were clearly correlated to dosage after 3 weeks of treatment. After 8 weeks, this correlation persisted for thioridazine but not for thiothixene. By that time, plasma levels of thiothixene had decreased to about 30% of the initial value, indicating strong enzyme action. 17 references. (Author abstract modified)

209830 Yorkston, N. J.; Zaki, Saniha A.; Malik, M. K. U.; Morrison, R. C.; Havard, C. W. H. Royal Northern Hospital, London N.7, England **Propranolol in the control of schizophrenic symptoms.** British Medical Journal (London). No. 5945(4):633-635, 1974.

A pilot study was undertaken using propranolol for psychosis to replicate previous research which had found the method to be effective in controlling schizophrenic symptoms. All schizophrenic symptoms remitted completely in 6 out of 14 adults who had not responded to phenothiazine drugs. Another patient improved markedly, four improved moderately, two had minimal or transient improvement, and one left the hospital unchanged. The six with complete remissions all began to improve within a few days of starting propranolol and the florid symptoms remitted completely after 3 to 26 days. They were stabilized on a daily dose of 500mg to 3,500mg of propranolol and at the time of writing had remained well for up to 6 months. Two patients relapsed severely within a few days. Toxic effects (ataxia, visual hallucinations, and confusional states) were related to the rate of increase rather than to the absolute dose of propranolol. After the procedure was modified, unwanted effects were usually mild or absent. 13 references. (Author abstract)

209905 Clark, Mervin L.; Huber, Wolfgang K.; Hill, Donna; Wood, Fredda; Costiloe, J. Paul. Central State Griffin Memorial Hospital, P.O. Box 151, Norman, OK 73069 **Pimozide in chronic schizophrenic outpatients.** Diseases of the Nervous System. 36(3):137-141, 1975.

The efficacy of Pimozide (PIM) used in maintenance and resocialization therapy with chronic schizophrenic outpatients, compared with placebo (PL) is described. In a double-blind clinical evaluation of maintenance therapy in chronic schizophrenic female outpatients, thioridazine, which was used as a standard drug to monitor the sensitivity of the experiment, in single daily doses was shown to be effective maintenance treatment compared with PL. Pimozide was also shown to be effective in a single oral dose and comparable overall to the standard drug. The experimental design was based on the anticipated retrogression of PL treated subjects during the 6 month study period. In addition, in some instances improvement over baseline evaluations was noted in both drug groups, particularly on global impression. Though some items of the Brief Psychiatric Rating Scale exhibited Drug:PL differences, the scale in general was felt to be rather insensitive for this kind of study. Social adjustment rating scales and drug side-effects are also discussed. 14 references. (Author abstract modified)

210500 Cazzullo, C. L.; Brambilla, F.; Cabibbe, F.; Martini, G.; Andreoli, V.; Mangoni, A. University of Milan Medical School, Milan, Italy **Drug resistance and bio-clinical factors in the response of schizophrenic patients to chlorpromazine.** Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(4):723-730, 1973.

The drug resistance and bioclinical factors in the response of schizophrenic patients to chlorpromazine were investigated before and after 40 days of treatment. No substantial differences were observed between Ss responding to treatment and those not responding with respect to fluid distribution and hormonal pattern; Ss who clinically improved with chlorpromazine treatment showed a very low output of chlorpromazine glucuronide in the urine while those who did not respond did not. It is suggested that these findings may be valuable, if confirmed by further studies, in predicting whether a patient will respond to chlorpromazine treatment by measuring the urinary output of chlorpromazine glucuronide. 24 references. (Journal abstract modified)

210510 De Natale, F. Ospedale Psichaitrico Provinciale "L. Mandalari", Messina, Italy /**A clinical-experimental study on the use of sulpiride in a group of chronic schizophrenics (first note).** Studio clinico-sperimentale sull'impiego della sulpiride in un gruppo di schizofrenici cronici (prima nota). Riv. Sper. di Frenistria e Med. Legale delle Alienazioni Ment. (Reggio). 97(4):889-903, 1973.

Sulpiride was administered to a group of chronic schizophrenics in intramuscular doses of 300mg-800mg/day and 400-1000mg/day/os. Preliminary results show very good and good improvement in over 50% of the cases. Sulpiride was well tolerated, even with high doses. Symptoms which responded particularly well to the effect of sulpiride included: autism, dysperceptive disturbances and delirium. 18 references.

210897 Bergen, J. R.; Mulhall, S.; Moorman, P. Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545 **Comparison of 3,4-dimethoxyphenylethylamine treated plasma from chronic schizophrenics and controls.** Research Communications in Chemical Pathology and Pharmacology. 10(2):331-335, 1975.

A comparison of 3,4-dimethyl 3,4-dimethoxyphenylethylamine treated plasma from chronic schizophrenic patients and controls is presented. Plasma samples were collected from chronic schizophrenic patients not on drug therapy and from nonpsychotic hospital volunteer controls and monoamine oxidase inhibitor (MAOI) pretreated mice who were then aggregated for 4 hours, the two kinds of plasma produced results so similar that no differences between them could be observed. Doubling the amount of plasma and DMPEA likewise failed to differentiate plasma origin. In our hands no differentiation between plasma samples from control subjects and schizophrenic patients could be determined under the conditions employed. 5 references. (Author abstract)

211304 Nishiura, Masanaka; Kimura, Sadamu; Aoki, Naotaka. Kansai Medical College, Japan. **Use of a new psychotropic drug, clofluperol for the treatment of chronic schizophrenic patients.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(4):446-452, 1974.

The effect of clofluperol on chronic schizophrenia was studied, based on experiment in which 23 patients with an average schizophrenic history of 17 years and one patient with recent onset of schizophrenia were treated with this drug for 18-135 days. Differential positive effects observed in each patient are described. Side-effects such as insomnia, tremor, salivation, nausea, vomiting and loss of appetite were observed in most of the patients. In two patients, increase in the dosage of this drug eliminated side-effects. All side-effects were eliminated by treatment with minor tranquilizers and antiparkinsonism agents.

211339 Otsuka, Tatemasa; Kumashiro, Hisashi; Mizushima, Shigemi; Maruko, Kazuo; Koizumi, Nobusuke; Umino, Yukihiro. Fukushima Prefectural Medical College, Japan **The effect of L-dopa on schizophrenia.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(6):629-637, 1974.

The effect of L-dopa on schizophrenia was studied, based on an experiment in which 22 chronic schizophrenic patients with hypoactivity and dull emotion as main symptoms. Ss were orally treated with L-dopa for 30-540 days along with other psychotropic drugs such as chlorpromazine, thioridazine, clothiapine, perphenazine, haloperidol, floropipamide, methylperidol, etc. The results show that seven showed remarkable improvement of their symptoms and could leave the hospital, four showed temporary improvement, seven showed no change, and four showed aggravation. The drug was more effective on younger patients, and effects appeared 5-10 days after the beginning of the drug treatment. L-dopa improved communication, volition and emotional expression among the patients with hebephrenia and catatonic type of schizophrenia; however, those with paranoid type of schizophrenia tended to show aggravation. Negative side-effects included loss of self-control, increase of sexual drive, hallucination, headache, irritation and dizziness, but these disappeared after a decrease in dosage or termination of treatment. 26 references.

211436 del Giudice, Joseph; Clark, William G.; Gocka, Edward F. Los Angeles County Mental Health Services, 1525 Euclid Ave., Santa Monica, CA 90404 **Prevention of recidivism of schizophrenics treated with fluphenazine enanthate.** Psychosomatics. 16(1):32-36, 1975.

Data are reported from studies on the use of fluphenazine enanthate in preventing recidivism of discharged schizophrenic patients. A small and statistically insignificant placebo effect associated with the regular administration of a placebo injection by a visiting nurse was demonstrated. A highly significant increase in the probability of remaining out of the hospital was associated with the administration of injectable fluphenazine enanthate to schizophrenics who respond to fluphenazine, when compared to schizophrenics given the oral form, fluphenazine dihydrochloride. 6 references. (Author abstract)

211437 Van Putten, Theodore; Mutalipassi, Louis R. UCLA School of Medicine, Los Angeles, CA **Fluphenazine enanthate induced decompensations.** Psychosomatics. 16(1):37-40, 1975.

Nine schizophrenic patients who experienced dramatic exacerbations of their original psychosis on fluphenazine enanthate in conventional dosages are reported. The exacerbations of psychosis appear to be extrapyramidally based, and can be reversed by intramuscular biperiden (Akineton), an anticholinergic drug. Response to biperiden is so prompt that it can be used as a diagnostic test. 20 references. (Author abstract modified)

212238 Astrup, C.; Grimsgard, A.; Hebnes, K.; Kruse-Jensen, A.; Lid, M. Tromsoe University, Tromsoe, Norway **A study of flupenthixol decanoate and pipotiazine undecylenate in schizophrenics.** Acta Psychiatrica Scandinavica (Kobenhavn). 50(5):481-491, 1974.

Forty three schizophrenic inpatients were treated with flupenthixol decanoate or pipotizine undecylenate during a period of 8 months. The patients were evaluated in a double-blind study lasting for 2 months. The calculated daily dosage of both drugs was 6mg. The trial started with 4 week intervals between the injections, which had to be decreased to 2 weeks for most patients during the open trial. No significant therapeutic differences could be established between the two drugs in the double-blind trial. All the laboratory data were normal, and the local tolerance was excellent. Eighteen patients were improved, 14 unchanged and 11 worse after 8 months of treatment. The improvement was predominantly due to less inhibitory and paralyzing side-effects than with previous sedative oral neuroleptic medication. An importan feature was that 12 patients, unwilling or unreliable in taking oral drugs, could be discharged as improved on stable medication. 14 references. (Author abstract)

212491 Carney, M.; Sheffield, B. no address **The long-term maintenance treatment of schizophrenic out-patients with depot flupenthixol.** Current Medical Research and Opinion. 1:423-426, 1973.

A report on the long-term maintenance treatment of schizophrenic outpatients with depot flupenthixol was developed from practical observation of 148 subjects (78 men and 67 women) over a period of 14 months. The patients were classified as 109 paranoics, 32 hebephrenics and 4 catatonics. The dosage was between 30 and 120mg every 3 weeks. Only five patients relapsed but undesirable effects were observed in 43% of the cases: parkinsonism, akathisis, moderate depression and hypomania. In comparison with fluphenazine, this drug was found to be a more powerful antideliriant. Depressive phases were noted in 6% of cases in two homogeneous groups of patients, while psychotic relapses were similar in both groups. Akathisis, however, was less prevalent with the new drug, and the patients treated with it were more active and sociable. Fluphenazine was classed as a better treatment for paranoid schizophrenics of a very aggressive nature.

213294 Yamanishi, Etsuro; Matsumoto, Eizon; Tomioka, Takeshi; Sato, Michiaki; Yamabata, Yasushi; Funasaka, Kazuhiko. Takarazuka Mita Hospital, Japan **Clinical experience of fluphenazine enanthate in treatment of schizophrenic patients.** Medical Consultation and New Remedies (Tokyo). 10(2):403-412, 1973.

The effect of fluphenazine enanthate on schizophrenia was studied, based on an experiment in which 18 patients with chronic schizophrenia were treated with this drug and with other psychotropic drugs and anti-Parkinsonism agents. Fluphenazine was effective in 55.6% of the patients, and especially effective on hallucination and delusion, followed by improvement in autistic tendencies and disorders in communication and interpersonal relationships. Anti-Parkinsonism agents eliminated autonomic nervous system disturbance and extrapyramidal syndromes in all patients except two, in whom termination of treatment of fluphenazine was required. A minor case of decreased blood pressure was observed; however, no other significant side-effects were evident. 8 references.

09 DRUG TRIALS IN AFFECTIVE DISORDERS

205601 Kabes, J.; Taussigova, D.; Dostal, T.; Vinar, O. Institute of Psychiatry, Praha 8-Bohnice, Czechoslovakia **L-dopa and tricyclic antidepressants in affective disorders. A pilot study.** Activitas Nervosa Superior (Praha). 16(3):186-188, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, reports a study in which four female patients suffering from severe depressive symptomatology treated with L-dopa were examined. They did not respond to the combination of nortriptyline and amitriptyline in the total dose of 250mg per day administered for 1 month at least. After this period L-dopa was added to the antidepressants. In all patients we ob-

served a marked improvement of the depressive symptoms during and after L-dopa treatment periods. In two patients a full remission has been achieved, the remaining two had some residual symptoms. In one patient after the withdrawal of L-dopa the depressive symptomatology reappeared but after another L-dopa period a full remission followed. There appeared no paranoid symptoms, hypomania or any other psychiatric complication. Nausea and rarely vomiting were the only side-effects. 12 references.

205602 Zimanova, J.; Vojtechovsky, M. Hospital for Mental Diseases, 411 85 Horni Berkovice, Czechoslovakia **Sleep deprivation as a potentiation of antidepressive pharmacotherapy?** Activitas Nervosa Superior (Praha). 16(3):188-189, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, reports an experiment in which sleep deprivation was examined as a potentiation of antidepressive pharmacotherapy. A favorable antidepressive effect of sleep deprivation was reported. Deterioration of mood was much more frequent. A shift of depression into mania in two patients with a bipolar type of depression was found. 1 reference.

205607 Soucek, K.; Zvolsky, P.; Krulik, R.; Filip, V.; Vinarova, E.; Dostal, T. Medical School of Charles University, Praha 2, Ke Karlovu 11, Czechoslovakia **The levels of lithium in serum and in red blood cells and its ratios in manic-depressive patients.** Activitas Nervosa Superior (Praha). 16(3):193-194, 1974.

At the 16th Annual Psychopharmacological Meeting, examinations of lithium levels in 63 patients of various stages of manic-depressive psychosis (both bipolar and unipolar forms) were reported. The comparison of results in the sample showed that the beginning of the manic phase was followed by a decrease of lithium concentration both in plasma and red blood cells, the latter being statistically significant. The concentrations of lithium were higher even during remission of unipolar depressive forms in comparison with manic phases. With bipolar forms there was an increase of concentrations in the depressive phase in comparison with values in the manic phase. The results suggest that during affective psychosis, in addition to the changes of extracellular concentrations of lithium, there are also changes of its intracellular concentrations which are probably more sensitive. 2 references.

205608 Zvolsky, P.; Vinarova, E.; Dostal, T.; Soucek, K. Research Psychiatric Unit, Charles University, 128 21, Praha 2, Ke Karlovu 11, Czechoslovakia **Family history of manic-depressive and endogenous depressive patients and clinical effect of treatment with lithium.** Activitas Nervosa Superior (Praha). 16(3):194-195, 1974.

At the 16th Annual Psychopharmacological Meeting, a study of the morbidity risk of psychic disorders in the families of patients suffering from primary affective disorder estimated from the aspect of the lithium effect was reported. A high morbidity risk of psychic disorder in patients was found. The question of whether lithium acts more or less specifically in patients of special subgroups of primary affective disorders or has the best effect on patients of the most expressed basic disorder was discussed. 2 references.

205609 Bily, J.; Hametova, M.; Hanus, H.; Polackova, J. Psychiatric Clinic, Medical Faculty Hradec Kralove, Czechoslovakia **Some specificities in the course of maniomelancholic psychosis during lithium therapy.** Activitas Nervosa Superior (Praha). 16(3):195-196, 1974.

At the 16th Annual Psychopharmacological Meeting, a study of the course of mania-melancholic psychosis during lithium therapy was reported Additional treatment was gradually less required and for those patients who had been treated for more than 3 years, lithium treatment alone would suffice for nearly 40%. These results indicate that the full effect of lithium therapy sets in later than in 1-3 years. 2 references.

205610 Mullerova, S.; Novotna, J.; Rehan, V.; Skula, E. Olomouc, Mozartova 21, Czechoslovakia **Lithium treatment of behavioural disturbances in patients with defective intellect.** Activitas Nervosa Superior (Praha). 16(3):196, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting describes an investigation in which a random sample of 20 oligophrenics, the influence of lithium was studied by clinical observation, by a psychologist and in laboratory findings (of 16 patients). The sample included 8 debils and 12 imbeciles. Behavior and adaptability was assessed with a questionnaire which was administered three times. Between the first and second measurement there was no significant difference. A comparison of the first and third measurement showed a significantly improved adaptability. The increase in variance at the second administration signals a wider scale of individual responses to treatment, while the decrease in variance at the third administration of the questionnaire signifies a stabilization. It was found that lithium exercised a favorable effect on oligophrenic patients. It proved significantly sociably and induced in four patients changes in emotivity.

205616 Zapletalek, M.; Pazdirek, S.; Hubsch, T.; Strnad, D. Psychiatric Clinic, Medical Faculty Hradec Kralove, Czechoslovakia **Clinical experience with clozapine in psychoses.** Activitas Nervosa Superior (Praha). 16(3):203-204, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, reports the effect of clozapine in a group of 34 patients. The drug appears to be most effective in anxiety and fear, tension, delusions, hallucinations, hostility, unusual thought contents, disorientation and less effective in depressive moods, emotional shallowness, restlessness, thought disintegration and negativism. The drug is relatively less effective in motor inhibition, mannerism, blunted affect, sense of guilt and megalomania. All the symptoms evaluated, with the exception of magalomania and concern with one's somatic state, show statistically significant differences. 6 references.

205929 Mellerup, Erling T.; Plenge, Per; Rafaelsen, Ole J. Psychochemistry Institute, Rigshospitalet, University of Copenhagen, 9, Blegdamsvej, DK-2100, Copenhagen, Denmark **Lithium and insulin: effects on carbohydrate and electrolyte metabolism.** Danish Medical Bulletin (Copenhagen). 21(3):88-92, 1974.

The numerous effects of lithium have emphasized the problem of identifying those which may be pertinent with respect to the use of lithium in manic-depressive psychosis. Comparative studies of other psychoactive drugs or agents which have physiologically similar effects to those of lithium may be helpful in this connection. Insulin and lithium have some effects in common, and a relationship between diabetes and manic-depressive psychosis has been suggested. Literature related to these topics is reviewed in order to illustrate the value of comparative studies with respect to the design of further experimental and clinical investigations. 57 references. (Author abstract)

206146 Noyes, Russell, Jr.; Dempsey, G. Michael. Dept. of Psychiatry, Univ. of Iowa College of Medicine, 500 Newton

Rd., Iowa City, IA 52242 **Lithium treatment of depression.** Diseases of the Nervous System. 35(12):573-576, 1974.

The evidence supporting lithium's antidepressant effect and its implications is reviewed and discussed. A review of all studies of lithium treatment of depression in both controlled and uncontrolled trials yielded the fact that, of the more than 300 depressed patients treated with lithium, over half have received benefit. However, a number of methodological deficiencies, including inadequate dosage, a broad dosage range, the absense of placebo control groups, and an inadequate duration of treatment are noted in interpretation of the results. Nonetheless, lithium appears to be an effective and safe treatment for depressions of the bipolar variety. The proven efficacy of lithium maintenance in the prevention of an attentuation of recurrent episodes of manic-depressive illness is cited as further evidence of significant antidepressant action on the part of the drug. Therefore, although lithium's use as an antidepressant now appears established further exploration is advocated to determine its specificity. 35 references.

206333 Chernik, D. A.; Mendels, J. Div. of Medical Affairs, Hoffmann-La Roche, Nutley, NJ **Longitudinal study of the effects of lithium carbonate on the sleep of hospitalized depressed patients.** Biological Psychiatry. 9(2):117-124, 1974.

The effects of 900mg/24 hr to 2400mg/24 hr lithium carbonate on the sleep of 10 hospitalized depressed patients for a total of 332 nights (baseline and drug nights) were studied. Lithium carbonate produced a significant decrease in wakefulness and in the lightest stages of sleep (Stage 1) together with a significant increase in the deeper stages of sleep (Stages 3 and 4). All 10 patients had a decrease in Stage 1 sleep and some increase in Stages 3 and 4. Further, nine out of 10 patients had a decrease in wakefulness. Thus, in general, sleep was improved with the administration of lithium therapy. However, lithium also produced a significant decrease in REM sleep, but since this was somewhat elevated prior to the administration of lithium carbonate, the mean levels following drug administration were close to the lower limit of the range found in normal subjects. A similar improvement or "normalization" of sleep was found with the administration of lithium carbonate to a young insomniac subject. 13 references. (Author abstract modified)

206366 Johnstone, Eve C.; Marsh, W. Dept. of Psychological Medicine, Southern General Hospital, Glasgow G51 4TF, Scotland **The relationship between response to phenelzine and acetylator status in depressed patients.** Proceedings of the Royal Society of Medicine (London). 66(9):947-949, 1973.

At the December 12, 1972 meeting of the Royal Society of Medicine, the response of 72 depressed patients to phenelzine was compared with their response to placebo, and the relationship between acetylator status and effectiveness of this drug was also examined. The 72 patients tended to derive sustained benefit from this course of treatment. Slow acetylators responded to phenelzine to a significantly greater degree than did fast acetylators. In fast acetylators phenelzine is no better than placebo but in slow acetylators it is better to a highly significant degree. These new findings suggest that it is possible to predict response to phenelzine. 7 references.

206601 Askevold, Finn. Psychosomatic Department, Oslo University Hospital, Oslo, Norway **Involutional melancholia in males?** Psychosomatics. 15(4):170-173, 1974.

Involutional melancholia, which may occur in males between the ages of 45 and 59, is studied and patients with this disorder are compared to a normal group of men of the same age. Those suffering from this depressive state come from a high social stratum and are ambitious. However they exhibit a feeling of emotional deprivation and distance. They are socially hyperadapted with inhibition of aggression but not of self-assertiveness. Patients given doxepin for a period of a year have made a successful recovery. Most can return to work and resume a more active sex life and can accept their age induced lowered physical capacity. 23 references.

206696 Glatzel, J. Neuro-Psychiatrische Klinik, Johannes Gutenberg-Universitat, D-6500 Mainz, Germany **/Critical remarks on Tellenbach's concept of "Typus melancholicus"./** Kritische Anmerkungen zum "Typus melancholicus" Tellenbach. Archiv fur Psychiatrie und Nervenkrankheiten (Berlin). 219(2):197-206, 1974.

A critique, based on experiences with lithium therapy in the treatment of endogenous depression, is presented of Tellenbach's concept of melancholia, which describes the so called "Typus melancholicus" as an important factor in the pathogenesis of psychotic depression. During lithium therapy psychopathological symptoms of various types appear at first. Later there is a loss of those characterological symptoms which constitute Typus melancholicus. The conclusion is that Typus melancholicus, similar to masked depression, apparently represents a special subclinical type of endogenous depression and not the premorbid personality. 19 references. (Author abstract modified)

206939 Penna, Manoel W.; Lion, John R. Department of Psychiatry, Institute of Psychiatry and Human Behavior, University of Maryland School of Medicine, Baltimore, MD 21201 **Gilles de la Tourette's Syndrome and depression: a case report.** Diseases of the Nervous System. 36(1):41-43, 1975.

A case report of a 54-year-old male with Gilles de la Tourette's Syndrome is presented. The case illustrates the symptoms of sudden involuntary movements and coprolalia and the existence of an obsessive personality in the patient. He also had an electroencephalographic abnormality in the temporal lobe area which might suggest the possibility of a psychomotor epileptoid automatism, but there was no alteration in consciousness and no elaborate stereotypic movements as they have been described for this condition. The nature of the development of a depression of psychotic proportions is discussed, suggesting that it may have resulted from haloperidol treatment or that it may have been a separate and distinct depressive illness coincident with the treatment of the Gilles de la Tourette's Syndrome. 15 references.

207446 Shopsin, Baron; Gershon, Samuel; Thompson, Hyacinth; Collins, Patrick. Department of Psychiatry, Neuropsychopharmacology Research Unit, New York University Medical Center, 550 First Ave., New York, NY 10016 **Psychoactive drugs in mania: a controlled comparison of lithium carbonate, chlorpromazine and haloperidol.** Archives of General Psychiatry. 32(1):34-42, 1975.

A study of the effects of lithium carbonate, haloperidol, and chlorpromazine in a double-blind experiment with moderately to severely disturbed patients in a mental hospital is reported. It was discovered that lithium carbonate and haloperidol produced a highly significant improvement of manic symptoms while chlorpromazine only provided sedation. Of the three drugs, lithium carbonate acted more evenly on the entire manic picture with total normalization realized during active treatment; the majority of the manic patients on lithium met discharge criteria at study termination. Five tables dealing with

rating scales of the patients under each drug are included and shortcomings in the evaluation process are also noted. 20 references. (Author abstract modified)

207535 Nagashima, Masanori; Kido, Kosei; Yamaguchi, Takashi; Nagai, Hiroyuki; Todoroki, Shunichi. Department of Neuropsychiatry, Nihon University School of Medicine, Japan **Investigation of clinical effects of FK-880 (sulpiride) on manic-depressive illness.** Medical Consultation and New Remedies (Tokyo). 11(8):251-260, 1974.

The effect of sulpiride on manic-depressive illness was studied in 25 outpatients with depression treated with this drug (100-450mg/day) for 7-70 days. The drug had some favorable effect in 76% of the patient sample. Improvement in anxiety, irritation and difficulty in concentration was more frequently observed than in depression itself, and these effects were most frequently observed in patients with endogenous and neurotic depression. Decrease in inhibition appeared more quickly than improvement in emotion, but effects as a whole were all apparent within 1-2 weeks. Minor side-effects, such as sinitus, dermatitis, and akathisia were observed infrequently and usually disappeared without discontinuation of treatment. 9 references.

207554 Fujiwara, Joro; Ohara, Yasuro; Hirata, Junichiro; Otsuki, Saburo. School of Medicine, Okayama University, Japan **Four cases of depression treated by indoleacetic acid.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(4):414-420, 1974.

The cases of four patients treated with 5-hydroxy-L-tryptophan (L-5HTP) for endogenous depression are reported. The patients ranged in age from 46 to 61 years of age at initiation of treatment. Two Ss were classified as manic-depressives, another with Parkinsonism and depression, and the last with senile depression. The drug showed little success in treating the manic-depressive Ss but was markedly successful in eliminating depression in the other two Ss. The case histories of each patient with extensive followup data are summarized. 14 references.

207681 Dunner, David L.; Fieve, Ronald R. Department of Internal Medicine, New York State Psychiatric Institute, 722 West 168th Street, New York, NY 10032 **Affective disorder: studies with amine precursors.** American Journal of Psychiatry. 132(2):180-183, 1975.

The clinical antidepressant effects of L-tryptophan given alone and in combination with L-dopa in 12 patients with a diagnosis of primary affective disorder was assessed. Preliminary results did not demonstrate an antidepressant response when L-dopa was combined with L-tryptophan. The results also did not support the catecholamine or biogenic amine hypotheses of affective disorder. 30 references. (Journal abstract)

207719 Watanabe, Shosuke; Ishino, Hiroshi; Fujiwara, Jiro; Otsuki, Saburo. Dept. of Neuropsychiatry, Kawasaki Medical College, Kurashiki, Japan **Relationship between serum lithium level and clinical response to depression treated with lithium carbonate.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 28(3):167-177, 1974.

A double-blind study of the antidepressant effects of lithium carbonate compared with those of imipramine in which serum lithium levels were measured at weekly intervals, is discussed. The time lapse change of serum lithium levels, therapeutic effects, the relationship between lithium level and frequency of side-effects and/or occurrence of leukocytosis are discussed. Of the 25 Ss measured, 16 were supposed to have taken the drug regularly, six were to have taken the drug irregularly and three Ss were supposed to have discontinued drug intake. Effects of the drug on lithium responders and on nonresponders is discussed. Data show that serum lithium levels were well corresponded with lithium dosage, frequency of occurrence of side-effects was generally constant among Ss, and no relationship was found between the occurrence of leukocytosis and serum lithium levels. 18 references. (Author abstract modified)

207720 Ogura, Chikara; Okuma, Teruo; Uchida, Yasunori; Imai, Shiro; Yogi, Hideaki; Sunami, Yuzuru. Dept. of Neuropsychiatry, Tottori University School of Medicine, Yonago, Japan **Combined thyroid (triiodothyronine)-tricyclic antidepressant treatment in depressive states.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 28(3):179-186, 1974.

A combined treatment with tricyclic antidepressants and triiodothyronine made with 44 Ss in a resistant depressive state is reported. The combined treatment was markedly effective in 12 cases, effective in 17, slightly effective in six, ineffective in eight and aggravated one. The effect of the combined use appeared 3 to 4 days after treatment was started. Side-effects appeared in 43% of the cases, but the incidence is the same as that of tricyclic antidepressants alone. Examinations revealed no abnormal findings except for a mild rise and fall in blood pressure and a mild increase in pulse rate. Since the study revealed that the combined therapy is frequently effective for cases in which the tricyclic antidepressants did not produce a sufficient therapeutic effect and the period to the onset of the effect was short, it is hoped that further research will be carried out. 14 references. (Author abstract modified)

207764 Freyhan, Fritz A. 2015 R Street, NW, Washington, DC **On the controversy of prophylactic antidepressants.** Comprehensive Psychiatry. 16(1):1-5, 1975.

Present knowledge on the prophylactic treatment of affective disorders is assessed. Mention is made of insulin coma therapy for schizophrenia as well as lithium control. Etiological considerations are reviewed along with methodological ones regarding the effectiveness of lithium. Various clinical problems related to appraising the efficacy of lithium treatment are noted. 12 references.

208789 Nichiiki, Shozo; Izeki, Katsuhiko; Segawa, Yoshihisa; Ishii, Tomoyuki; Ishii, Kazuhiko; Nakaoka, Kiyohito; Kodama, Hisashi. Department of Neuropsychiatry, Hiroshima University, Hiroshima, Japan **Use of antidepressant E-330 (iprindole).** Medical Consultation and New Remedies (Tokyo). 11(8):263-269, 1974.

The effect of E-330 on depression was evaluated in 20 patients with various depressive diagnoses treated with this drug (45-90mg/day) for from 11 days to 8 weeks. The drug showed some favorable effect on 60% of the sample. E-330 was considerably weaker than the tricyclic antidepressants in treating depression accompanied by strong anxiety and irritation. The drug was most effective in endogenous depression, improvements occurring within 2 weeks of beginning therapy. Side-effects appeared in 35% of the sample, but only one patient had to drop therapy due to these effects. 5 references.

208917 Mendels, J.; Frazer, A.; Secunda, S. K.; Stokes, J. W. Philadelphia V.A. Hospital, Philadelphia, PA 19104 **A study of electrolyte and biogenic amine metabolism in manic-depressive illness.** International Pharmacopsychiatry (Basel). 9(4):206-217, 1974.

Erythrocyte, electrolyte (sodium, potassium and magnesium) and urinary amine metabolism (norepinephrine, dopamine, 3-methoxy-4-hydroxymandelic acid (VMA), and 5-hydroxyindoleacetic acid (5HIAA)) concentrations were studied over time in a manic-depressive patient treated with lithium carbonate. The alterations in these substances, their correlations with each other and with the patient's clinical condition are presented and discussed in terms of possible interactions between electrolyte and biogenic amine metabolism in depression. 39 references. (Author abstract)

209070 Benaim, Silvio; Lappin, Frank. Royal Free Hospital, London **/Therapy with lithium salts in manic-depressive illnesses./** La terapia con sali di litio nelle malattie maniaco-depressive. Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(3):677-691, 1973.

The use of lithium salts in treating manic-depressive illnesses is discussed. Lithium has been successfully used in treating manic and hypomanic states, in cases of depression with bipolar illnesses combined with tricyclic drugs or electroshock, and as a prophylactic in patients who have frequent relapses. Lithium is also useful in treating unipolar illnesses. On the basis of results obtained with a population of 101 unipolar and bipolar patients, lithium was found to have a prophylactic effect. The possible side-effects of lithium therapy and toxic reactions are discussed. Possible explanations of the mechanism of lithium include: alterations in electrolyte metabolism both in depressive states; increases in the level of plasma cortisol; and changes in serotonin metabolism in the brain. These hypotheses still do not explain how lithium can normalize neuronic excitability or neuronic hypoexcitability in depression.

209082 Snaith, R. P.; McCoubrie, M. Stanley Royd Hospital, Aberford Rd., Wakefield, Yorkshire WF1 4DQ, England **Antihypertensive drugs and depression.** Psychological Medicine (London). 4(4):393-398, 1974.

A survey of the incidence of depressive illnesses in patients taking hypertensive drugs is reported. The Wakefield Self-Assessment of Depression Inventory was used for the 30 Ss in the trial. Results show no relation between the administration of methyldopa or of other drugs and depressive illness. The findings are an indication that adverse psychiatric effects of drugs for hypertension, and methyldopa in particular, may be less common than is sometimes supposed. Further research is recommended to clarify the matter. 25 references. (Author abstract modified)

209122 Gianelli, A.; Jogan, E.; Rizzo, M. Istituto Psichiatrico Provinciale "Paolo Pini", Milan **/Preliminary results on the clinical use of a slow-release preparation of lithium salts./** Risultati preliminari sull'uso clinico di una preparazione ritardo di sali di litio. Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(2):344-355, 1973.

Seventeen patients suffering from affective disorders were treated with a slow release preparation of lithium salts (lithium sulfate) for a minimum of 2 months to a maximum of 29 months. Given the brevity of treatment in some of the Ss, it is impossible to formulate valid clinical conclusions on the therapeutic effects. The reduction of side-effects and the constancy of serum levels allowed reduction of the number of doses to 1-2 per day. The slow absorption of the compound reduces variations in the serum concentration of lithium due to repeated administrations and consequently the side-effects connected principally with the high levels attained during the absorption phase. These data indicate that the use of a slow release preparation of lithium salts will allow extending therapy with patients who cannot tolerate immediate absorption. 18 references. (Journal abstract modified)

209144 Cavalca, G. G.; Covezzi, E.; Boncinelli, A. Clinica delle Malattie Nervose e Mentali dell' Universita di Milano, Milan, Italy **/Clinical experiences in treating depressed patients with a combination of tricyclic drugs and thyroid extract./** Esperienze cliniche del trattamento di pazienti depressi con abbinamento di farmaci triciclici e estratti tiroidei. Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 98(2):271-300, 1974.

Clinical experiments concerning the treatment of depressed patients with a combination of tricyclic drugs and thyroid extracts were reported. The efficacy of thyroid hormones in potentiating the therapeutic effect of antidepressants allows hypothesizing that hormonal treatment which balances the hypophysithyroid endocrinal secretion contributes to the normalization of diencephalic function. It is concluded that thyroid extracts can be usefully added to imipramines and amitriptylines in treating psychotic manifestations of the depressive type. Their specific action seems to be the reduction of the latency time between the initiation of therapy and the appearance of improvement. 30 references.

209148 Lampugnani, E.; Minazzi, M. Ospedale Provinciale di Vimercate, Vimercate, Italy **/Clinical-electroencephalographic data in depressed patients treated with Anafranil./** Rilievi clinico-elettroencefalografici in pazienti depressi trattati con Anafranil. Riv. Sper. di Freniatria e. Med. Legale delle Alienazioni Ment. (Reggio). 98(2):388-396, 1974.

The optimal dosage of Anafranil for the individual patient was investigated. Electroencephalographic (EEG) alterations, with the dosage studied, were present in the majority of cases (11 out of 15) and began with an infused dose of 75mg in 15 minutes. Subsequent therapy, begun with a daily dose of 75mg administered in one infusion in the morning, had to be modified between the fifth and tenth day. No rigid correlation between clinical efficacy and EEG modifications emerged. A positive relationship was revealed between EEG "plasticity" and therapeutic outcome. The use of an EEG control during the first administration of the drug seems valid for furnishing elements for a prognostic judgment without giving any sure indications of the optimal dosage. 16 references.

209332 Kielholz, P. no address **/Depressive condition. Perception, evaluation, treatment./** Depressive Zustande. Erkennung, Bewertung, Behandlung. Bern, Verlag Hans Huber, 1972. 304 p. Fr. 32.

General clinical, biochemical, and statistical research problems of depression are discussed. Pharmacologic and clinical research on new antidepressants is described.

209392 Hasegawa, Kazuo; Schou, Mogen. no address **The lithium prophylactic treatment of recurrent endogenous affective disorders.** Clinical Psychiatry (Tokyo). 15(7):787-796, 1973.

The literature on the lithium prophylactic treatment of the recurrent endogenous affective disorders is reviewed. Lithium definitely has prophylactic effects on recurrent manic-depression or periodic endogenous depression. Dosage of lithium must be determined individually, and the serum lithium level should be constantly checked since low lithium concentration results in recurrence of symptoms and high concentration may induce lithium poisoning and death in some cases. Lithium treatment may also induce side-effects. A further study is

necessary to find out the mechanism of lithium effects. 40 references.

209413 Watanabe, Shosuke; Taguchi, Kanzo; Nakaya, Koji; Otsuki, Saburo. Department of Neuropsychiatry, Okayama University School of Medicine, Okayama, Japan **Clinical effects of lithium carbonate on depressive states.** Clinical Psychiatry (Tokyo). 15(7):781-786, 1973.

The effect of lithium carbonate on depression was evaluated in 55 patients with diagnozed depression, involutional melancholia, or circular depression. The drug was most effective in depression, but all groups responded positively in 50% of those treated. Lithium was generally effective within 10 days of initiating treatment at a blood level of 0.47 mEq/1. No significant correlation was observed between lithium effects and type of depression, characteristics of depressive state, and serum lithium concentration. 19 references.

209437 Haskell, David S.; DiMascio, Alberto; Prusoff, Brigitte. Psychiatry Dept., Boston Univ. School of Medicine, Boston, MA **Rapidity of symptom reduction in depressions treated with amitriptyline.** Journal of Nervous and Mental Disease 160(1):24-33, 1975.

The changes in the pattern and timing of 14 sumptoms appearing in 172 acutely depressed women undergoing drug treatment for 4-6 weeks before receiving psychotherapy were investigated. A group of depressed women treated with amitriptyline was studied with particular attention to the speed of response in different symptoms of depression and in psychotic compared to neurotic depressives. The findings showed rapid improvement in suicidal feelings, insomnia, and anorexia, but slower and more gradual improvement in impaired work and interests, retardation and pessimism and hopelessness. Psychotic depressives did not show substantial improvement until the third week of treatment, whereas neurotic depressives improved markedly within the first week. It is suggested that the psychotic classification may be more useful as a predictor of speed of response than as a predictor of final treatment outcome. 16 references. (Author abstract modified)

209901 Ayd, Frank J., Jr. Taylor Manor Hospital, Ellicott City, MD 21043 **Maintenance doxepin (Sinequan) therapy for depressive illness.** Diseases of the Nervous System. 36(3):109-114, 1975.

The efficiency and safety of long-term doxepin maintenance therapy was studied, using 32 depressive patients. Most of the subjects were beyond middle age and suffered from chronic melancholia. Results of "drug holidays" as long as 2 weeks without a relapse are reported. Tolerance results, clinical observations and laboratory investigations are also provided. It is concluded that doxepin, even in large doses over 52-93 months, had no demonstrable deleterious effect on the blood, liver, or kidney in the patients, thus long-term maintenance can be effective and safe. Reference is made to other maintenance regimens using other antidepressants. A table indicating daily dosage range, total dosage, and duration of treatment for each patient is also included. 6 references. (Author abstract modified)

210126 Rosier, Y. A.; Broussolle, P.; Fontany, M. no address **/Lithium gluconate: systematic and factorial analysis of 104 observations over 2.5-3 years in patients presenting cyclothymic or dysthmic disorders./** Gluconate de lithium: analyse systematique et factorielle de 104 observations, faites depuis deux ans et demi a trois ans chez des malades regulierement suivis et presentant des cyclothymies ou des dysthymies periodiques. Annales Medico Psychologiques (Paris). 1(3):389-397, 1974.

A factorial analysis of 104 patients suffering from affective disorders, and treated with lithium gluconate (LG) showed that LG was effective in preventing relapses in 97% of the cases. Results are for true cyclothymic disorders and not isolated mood disturbances, and also for psychotic states of relapse presenting a manic or depressive aspect as part of a more complex whole. It is recommended that treatment begin in the "interphase" and the preferred dosage is specified. It the is suggested that lithium levels be checked after 3, 4, 15, 30 and 60 days. Several neurological disturbances are predicted, including tremor, abnormal movements, nausea, and moderate weight gain. It is noted that Ss with a history of thyroid should be treated with caution, and that cardiac patients should have their renal function monitored carefully. It is asserted that once an adequate lithium level has been reached it will stabilize.

210128 Sichel, J.-P.; Fonlupt, V.; Roueff, E. no address **/Experimentation with the intravenous form of amitriptyline with 40 patients./** Experimentation de la forme intraveineuse de l'amitriptyline chez 40 malades. Annales Medico Psychologiques (Paris). 1(3):407-420, 1974.

Forty patients suffering from affective disorders were experimentally treated with an intravenous form of amitriptyline. Very satisfactory results were found in 19 cases (47%), satisfactory in 13 (33%), unsatisfactory in four (10%), and four (10%) were insignificant. Recommended dosage is from 50 to 100mg. Oral administration was satisfactory, with a dosage of 10mg. The average maintenance dosage was 50-75mg orally for 15-20 days.

210213 Fazio, C.; Andreoli, V.; Agnoli, A.; Casacchia, M.; Cerbo, R. 1a Clinica Malattie Nervose e Mentali dell'Universita, 00100 Rome, Italy **/Therapeutic effects and mechanism of action of S-adenosil-L-methionine (SAM) in depressive syndromes./** Effetti terapeutici e meccanismo d'azione della S-adenosil-L-metionina (SAM) nelle sindromi depressive. Minerva Medica (Torino). 64(29):1515-1529, 1973.

An open and double-blind clinical trial of the therapeutic effects of S-adenosyl-l-methionine (SAM) was performed with 49 depressive patients. SAM is physiologically synthesized in the central nervous system and is present in various concentrations in different areas of the brain. The donor substance is activated by methyls and is involved in neurotransmitter synthesis and catabolism processes. SAM injected into systemic circulation rapidly crosses the blood-brain barrier and is thus a potential nerve drug in the management of depression. The drug manifested a rapid and intense antidepressive effect, with positive results in over 80% of the cases. A specific rating scale (Hamilton's scale) for depression was used in evaluating the experiment. 62 references. (Journal abstract modified)

210241 Watanabe, Shosuke; Doi, Toru; Tamaoki, Sachihiro; Shomori, Atsuko; Hanaoka, Masanori; Wake, Akira; Aoyama, Kazuo; Fujiwara, Jiro; Nakajima, Yoshihiko. Department of Neuropsychiatry, Okayama University, Japan **A double-blind comparison of lithium carbonate and imipramine in the treatment of depression.** Clinical Psychiatry (Tokyo). 16(9):785-794, 1974.

The effects of lithium carbonate (Li) and imipramine (Im) on depression were compared, based on a double-blind experiment in which 45 patients with depression were treated with either Li or Im for 5 weeks. No significant difference was observed in the overall affects of the two drugs, although Li was slightly more effective. Relief from depressive feelings and

loss of bodyweight were observed more with Li treatment, and Im was slightly more effective on anxiety and bad temper. Li and Im both induced side-effects, such as headache, loss of appetite, nausea, dry mouth, tremor, urgency and polyuria. Li induced leucocyte increase in some of the patients. 12 references.

210501 Mangoni, A.; Cabibbe, F.; Cazzullo, C. L.; Meani, E.; Andreoli, V.; Villani, F. University of Milan Medical School, Milan, Italy **Clinical-biological correlations in schizo-affective patients treated with lithium carbonate and haloperidol.** Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(4):731-737, 1973.

The results of treating seven patients suffering from schizo-affective psychoses with lithium carbonate for 2 weeks and with lithium plus haloperidol for another 2 weeks are reported. The lithium had a therapeutic effect on the affective symptoms; the addition of haloperidol after 2 weeks resulted in an improvement in the whole psychotic picture. There was a drop in sodium levels in the blood during both methods of treatment. Intracellular water volume increased after treatment with lithium alone and decreased after treatment with lithium and haloperidol. The meaning of the changes in intracellular water volume in psychotic patients is discussed. 15 references. (Journal abstract modified)

210507 Rizzo, M.; Standen, S. M.; Giannelli, A.; Jogan, E.; Morselli, P. L. Ospedale Psichiatrico Provinciale "Paolo Pini", via Ippocrate 45, Milan, Italy **/Some observations on the correlations between plasma levels of monomethylated tricyclic antidepressants and therapeutic effects./** Alcune osservazioni sulle correlazioni fra livelli plasmatici degli antidepressivi triciclici monometilati ed effetti terapeutici. Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(4):837-861, 1973.

Correlations between plasma levels of monomethylated tricyclic antidepressants and their therapeutic effects were investigated. The drugs used were nortriptyline (NTP), amitriptyline (AMI), desmethylimipramine (DMI) and imipramine (IMI), administered alone or in combination. The following conclusions are drawn: marked variability in NTP and DMI blood levels independent of the dosage was observed; the decrease in plasma levels observed in six patients despite improvement in the clinical situation emphasizes the necessity and importance of periodically monitoring the plasma levels of the drug in patients on maintenance therapy after discharge from the hospital; a correlation seemed to exist between the average plasma levels of NTP and DMI and the therapeutic result; and no correlations were observed between side-effects and plasma values when the drugs were within the limits of 200ng/ml. 31 references.

210635 Sano, Isamu. Osaka University School of Medicine, Japan **Amines and disorders of the central nervous system.** Journal of the Japan Medical Association (Tokyo). 72(6):659-665, 1974.

The effects of L-5-hydroxytryptophan (L-5-HTP) on depression and parkinsonism are examined. Of the 174 depressive patients treated with from 100-300mg/day of L-5-HTP, over 80% showed complete or almost complete remission within 5 weeks. Some side-effects, particularly gastric, were noted when the drug was administered in powdered form, a condition alleviated by using tablets. The drug was only moderately effective in relieving the symptoms of parkinsonism.

210807 Groschel, W.; Kluge, H.; Zahlten, W.; Waldmann, K. -D.; Hartmann, W.; Glitschka, A.; Greger, J. Klinik fur Psychiatrie und Neurologie "Hans Berger" der Friedrich-Schiller-Universitat, Jena, Germany **/Comparative studies about serum electrolytes during lithium prophylaxis of affective disorders.** Vergleichende Untersuchungen zum Elektrolytverhalten im Serum bei Li-Prophylaxe zyklothymer Psychosen. Pharmakopsychiatrie Neuro Psychopharmakologie (Stuttgart). 7(6):300-306, 1974.

Changes of serum sodium, potassium and calcium in patients with affective disorder treated prophylactically with lithium salts in symptom free phases controlled over 6 to 24 months were examined. Eighty percent of all patients showed an increase of serum calcium by about 10%, undependent on the effective form. The changes of calcium followed those of lithium with a small time retardation. Potassium increased in about 50% of all patients investigated; 70% of these belonged to the bipolar and only 30% to the unipolar group. No significant changes in serum sodium could be observed. 16 references. (Author abstract modified)

210809 Arnold, L. E.; Krebs, G.; Knopp, W. Department of Psychiatry, Ohio State University, 1473 West 12th Avenue, Columbus, OH 43210 **Amphetamine treatment of paranoid obsessions: case report and biochemical implications.** Pharmakopsychiatrie Neuro Psychopharmakologie (Stuttgart). 7(6):322-327, 1974.

After unsuccessful treatment with thioridazine the successful treatment of a hospitalized obsessive - compulsive, paranoid adolescent with levoamphetamine is reported. Discontinuation was followed by relapse, and resumption by repeat improvement. This finding suggests that paranoid patients may suffer either an excess or deficit of dopamine or other catecholamine, and that those who claim neuroleptics make them worse may suffer a deficit. It is suggested that such cases may specifically indicate a catecholaminergic drug rather than an antidopaminergic neuroleptic, and knowledge of such individual differences may provide a rationale for more precise psychopharmacotherapy. 8 references. (Author abstract)

211432 Ban, Thomas A. Division of Psychopharmacology, McGill University, Montreal, Canada **Pharmacotherapy of depression -- a critical review.** Psychosomatics. 16(1):17-20, 1975.

A critical review is made of the pharmacotherapy of depression, therapy with tricyclic antidepressants and therapy based on biochemical hypotheses. It is concluded that there is no sufficient evidence to believe that there is a genetic and biochemical difference between bipolar and unipolar depressions, and that the primary choice of maintenance therapy in bipolar depression is with lithium salts and in unipolar depression with tricyclic antidepressants. As to affective disorder, systematic psychopharmacological studies with tricyclic antidepressants have provided sufficient data to hypothesize that in psychomotor retardation, catecholamines, and in sleep disturbance, indoleamines, may play an important role. 36 references. (Author abstract modified)

212161 Branzei, P.; Balan, G. Spitalul Clinic de Psihiatrie, Socola IASI, Soseaua Bucium 36, Romania **/Contributions to the study of the influence of lithium carbonate on the evolution of hyperthymic psychoses./** Contributions a l'etude de l'influence du carbonate de lithium sur l'evolution des psychoses hyperthymiques. Acta Psychiatrica Belgica (Bruxelles). 74(3):241-253, 1974.

The activity of lithium carbonate in 96 manic and melancolic patients was studied. Its efficacy in almost 75% of the cases is noted. The best results were observed in the acute manic episodes (hypomanic and manic states) and in the prevention of their periodic recurrence. Administered on a preventative basis during 3 years, lithium was active in 93% of hyperthymic syndromes. Good results were obtained in depressive episodes of cyclothymic patients; poor results were obtained in melancholic phases of manic-depressive patients; and there were no results in chronic melancholia. The study of 32 other patients has shown that lithium potentiates the action of neuroleptics. According to a regular check of lithium blood levels, the chronic administration of the drug was well tolerated if maintenance dosages did not exceed 800mg/day. Side-effects have been negligible in frequency and intensity and regress as soon as lithium is reduced or stopped. 34 references. (Journal abstract modified)

212162 Breulet, M.; Bourdouxhe, Suzanne; Parent, M.; Legros, J. J.; Bobon, J. Department de Psychiatrie, Clinique Notre-Dame des Anges, Universite de Liege, Liege, Belgium **/Clinical and neuroendocrinological study of TRH in melancholia./** Etude clinique et neuro-endocrinienne de la TRH dans la melancolie. Acta Psychiatrica Belgica (Bruxelles). 74(3):254-277, 1974.

Thyrotropin releasing hormone (TRH) was studied clinically and neuroendocrinologically in melancolics. A daily dosage of .5mg TRH was administrated during 10 days without any other threatment to three female and three male melancolic patients. Psychic energy was improved in two patients, and for a short time in the four other patients. Psychotonicity definitely increased in four patients, for a short time in the two others. Decrease of anxiety was observed in two patients, increase of anxiety in four patients. Despite the high dosages, TRH was well tolerated. There was no sign of hyperthyroidism from the clinical or the biological side. Analysis of the endocrinological data showed that: 1) the endogenous depressives of the present study had no disturbance of the hypothalamo - hypophyseal - thyroid function as compared to the normal values; and 2) the repeated injection of high dosages of TRH over 10 days did not induce detectable biological modifications of this function. 20 references. (Journal abstract modified)

212165 Berliner, Jacques. Centre de Guidance d'Ixelles, Rue d'Alsace-Lorraine 22, B-1050 Brussels, Belgium **/Testing Anatensol decanoate, a major neuroleptic, at the Ixelles Guidance Center./** Experimentation au niveau du Centre de guidance d'Ixelles d'un neuroleptique majeur: l'Anatensol decanoate. Acta Psychiatrica Belgica (Bruxelles). 74(3):305-316, 1974.

Repeated intramuscular injection of Anatensol decanoate, a major neuroleptic, in 18 psychotic patients was followed up by care at the Ixelles Guidiance Center in Brussels. A sufficiently positive response to generalized treatment was observed in all cases in which continuous intake of neuroleptics was necessary. Local and systemic tolerance of the drug, its incisive effect on psychomotor agitation and on delusions, its manageability, and the possibility of establishing regular contact in a supportive psychotherapeutic relationship, are cited as evidence of the success of such therapy. (Journal abstract modified)

212211 Bral, E. Latoratoire de l'hopital Sina, Teheran, Iran **/Study of 220 observations of Lithium therapy in depression cases in Teheran./** Etude de 220 observations de lithiumtherapie dans les etats depressifs a Teheran. Annales Medico-Psychologiques (Paris). 2(4):577-579, 1974.

The use of lithium therapy for depression cases was studied. Two hundred twenty cases were dosed with lithium prepared for classical dosage by flame photometry. A control population of 74 was also dosed. Forty six urinary lithium examinations were carried out. Normal seric and plasmatic results were .38-.59 and the urinary results were 1 mEq/l for Lithium. Of the 146 patients on lithium carbonate treatment, only one had suffered from secondary effects, and treatment was stopped. Maximum dose of seric lithium 1.5mEq/l was also well tolerated and the treatment was continued without difficulties. 5 references.

212213 Dreyfuss, L.; Lauras, A.; Hanon, E.; Housse, J. no address **/Atypical indication of lithium therapy./** A propos de quelques indications atypiques de therapeutique par le lithium. Annales Medico-Psychologiques (Paris). 2(4):585-599, 1974.

The extension of lithium treatments beyond manic-depressive psychosis to marginal psychotic forms was studied. Ten cases in which lithium treatments were prescribed are detailed. Use of lithium treatment in marginal cases was analyzed in five ways. Methodologically, it was noted that little is known about the psychological mechanisms of action of lithium. The evolution of certain melancholic traits into manic-depression was uncertain. Observational delay before lithium treatment was judged necessary in any case. Evolutively, psychometric tests proved to be of some use in determining the patient's condition, although certain key factors were beyond their reach, such as additional awareness of the manic-depressive structure. Criteria for charting the retaining of improvement are suggested and include nosographic, statistical and creative aspects of the personality. Time has not sufficiently elapsed to allow for accurate followup in this experiment.

212340 Watanabe, Shosuke; Ishino, Hiroshi; Otsuki, Saburo. Department of Psychiatry, Kawasaki Medical College, Kurashiki, Japan **Lithium ion and affective psychoses.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 28(4):267-305, 1974.

The literature on all clinical and fundamental studies of lithium in Japan since 1967 is reviewed. A number of studies indicate that lithium carbonate is effective in the treatment of manic-depressive psychosis (MDP) and in its prophylaxis, but for other diseases further study is needed. The mode of action of lithium ion in MDP is not known, but lithium has provided a new tool for biological studies on MDP. Lithium carbonate differs from other psychotropic drugs. Lithium can be used with safety under careful monitoring. Unsolved problems are the need to: clarify the characteristics of responders to lithium; study the effects of lithium on depression; evaluate the prophylactic effects of lithium and establish the maintenance lithium dosage for the Japanese; determine the therapeutic value of lithium in affective disorders other than MDP; establish specific therapy for lithium intoxication; and elucidate the exact mode of action and physiological role of the lithium ion. 177 references. (Author abstract modified)

212392 Gisselmann, A.; Marin, A. Service de Psychiatrie, C.H.U. de Dijon, 21033 Dijon Cedex, France **/A true antidepressant: 19 560 R. P./** Un antidepresseur vrai: le 19 560 R.P. Information Psychiatrique (Paris). 51(2):213-219, 1975.

The structural, biochemical, and pharmacological characteristics of 19 560 R. D.,a tricyclic antidepressant, are reviewed, and results of a clinical study of 50 women with various types of affective disorders are presented. Satisfactory results were obtained in 70% of the group, with only 4% exhibiting major side-effects. Treatment with 19 560 R. D. is ad-

vocated, as it is a fast acting antidepressant without sedative effects, is well tolerated by a majority of patients, precludes the need for prescription of multiple drugs, and is not contraindicated in cases with histories of glaucoma or urine retention.

212492 Soussen, G. no address **/The action of sulpiride in pure interpretive delerium./** Action du Sulpiride dans les delires interpretatifs purs. Psychologie Medicale (Paris). 5:901-909, 1973.

The interpretive delirum of Serieux and Capgras, which occurs the middle-aged or the very young in particular, was treated by sulpiride. The 15 Ss were administerd a dosage of 150-400mg/day. In at least one case, a young woman whose fantastic and imaginative personality suggested extreme sensitivity, the treatment resulted in suicide. It is concluded that the pharmacological action of sulpiride could be a reinforcement of the psychological tone, a stimulation of perceptual control, and their integration into the conscious, permitting the patients to fight "parsitic" ideas.

212518 Weissman, Myrna Milgram. Yale University **A follow-up study of female depressed outpatients who complete a randomized double blind prophylactic trial of antidepressants and high contact. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-26357 HC$13.50 MF$5.00 346 p.

Women who had completed 8 months of prophylactic antidepressant therapy and psychotherapy (high contact) for depression as part of a randomized clinical trial were followed up 6 months and 1 year after completion to determine problems arising in termination of treatment, to follow the clinical course and treatment experience and their predictors, and to see if prophylactic treatment had an enduring effect. Difficulties did arise in termination of treatment, with over 40% of the Ss continuing outpatient treatment in the followup. Hospitalization was rare, as was suicide. None of the maintenance treatments had an enduring effect, and a strong relationship existed between return of symptoms and receipt of treatment in followup. Patients tended to receive treatment in the followup which was similar to their maintenance treatment. Social dysfunction in the followup was related to the severity and chronicity of the acute symptoms and to premorbid social functioning. Upper social class patients and those initially more symptomatic received more treatment in the followup. The relationship of findings to previous research and implications for clinical care and health care policy are discussed. (Journal abstract modified)

212947 Nishikawa, Kisaku; Omine, Shigeji; Kashima, Haruo. Department of Neuropsychiatry, National Chiba Hospital, Japan **Therapeutic studies of depression with L-dopa.** Clinical Psychiatry (Tokyo). 15(11):1213-1222, 1973.

The effect of L-dopa on depression was examined in 13 patients treated with 500-750mg/day of this drug alone or in combination with diazepam or imipramine for 2 to 40 days. Seven patients responded favorably to L-dopa treatment. L-dopa frequently induced a manic state, but this side-effect was controllable with tranquillizers. L-dopa was noneffective in treating aggravated anxiety and irritation. 22 references.

10 DRUG TRIALS IN NEUROSES

205614 Nica, St.; Ciurezu, T.; Udangiu, L. Clinic of Psychiatry, Bucurest, Rumania **Results achieved with clozapine (Leponex) in the treatment of neuroses.** Activitas Nervosa Superior (Praha). 16(3):201-202, 1974.

At the 16th Annual Psychopharmacological Meeting, a study of the effectiveness of clozapine on neurotic symptomatology, particularly on sleep disturbances and anxiety, was reported. The drug induced sleep rather rapidly and awakening was not accompanied by sensations of heavy head. At the same time it had a favorable influence in cases with a tiresome oniric activity. The good tolerance, the absence of side-effects and the evident effect on sleep disturbance and anxiety indicates clozapine that is a suitable drug for antineurotic treatment of in- and outpatients. It is concluded that due to its psychopharmacological properties, Leponex (clozapine) is fully utilizable in the therapy of neurosis. 5 references.

205638 Boucek, J.; Vinar, O.; Novak, A. University Psychiatric Department, Institute of Psychiatry, Prague 8, Czechoslovakia **A controlled comparison of chlorazepate with oxazepam in neurotic anxiety.** Activitas Nervosa Superior (Praha). 16(3):239-240, 1974.

At the 16th Annual Psychopharmacological Meeting, a controlled comparison of chlorazepate with oxazepam in neurotic anxiety was presented. Data obtained in 62 patients were available for analysis. A decrease of the scores occurred during the treatment in the patients treated with both drugs. No statistically significant difference was found between the effects of the compared drugs. With the exception of very mild sedation in 4 patients, no side-effects were registered. 3 references.

206043 DeSousa, Alan; Choudhury, P. C. Grant Medical College, Bombay-8, India **Double blind trial of "sintamil" in depression.** Indian Journal of Psychiatry (Madurai). 16(2):159-164, 1974.

A double-blind between patients trial with Sintamil and imipramine was conducted. Treatment with Sintamil resulted in a favorable alteration in the depressive state in 68.97% as compared to 40.90% of the patients treated with imipramine. A satisfactory response was observed in 90% of the severe cases of depression treated with Sintamil, whereas only 29.41% of the patients with a similar degree of severity responded to imipramine. Sintamil was superior to imipramine in controlling sadness and anxiety, equal in somatic preoccupation and inferior in insomnia. The incidence of side-effects associated with Sintamil was lower than with imipramine. It is felt that because of these findings, Sintamil can safely be considered an effective agent in the treatment of depression. 5 references. (Author abstract modified)

206228 no author. no address **Agoraphobia** British Medical Journal (London). No. 5938:177-178, 1974.

The symptoms and management of agoraphobia are detailed. Agoraphobia has a definite onset, usually in the 20s or 30s, and the patient, usually a woman, develops symptoms of severe anxiety in public places. Management takes the form of an attempt to reduce the disability and to help the patient to make the most of life in spite of any disability which is resistant to treatment. Benzodiazapines and other anxiolytics are said to be of only limited benefit for the longstanding case, because of the development of tolerance; their most effective use is probably to help the patient to attend uncommon events such as weddings. A recent trial suggests that the monoamine oxidase inhibitor phenelzine may be helpful. There is also evidence that psychosurgery may be beneficial. The psychological technique of flooding, in which the patient is maintained in the feared situation for several hours until the anxiety wears off and he is able to relax in a formerly terrifying situation, is also recommended. 12 references.

206367 Kelly, Desmond. St. Georges Hospital Medical School, Atkinson Morley's Hospital, London SW20 0NE, England **Phenelzine in phobic states.** Proceedings of the Royal Society of Medicine (London). 66(9):949-950, 1973.

At the December 12, 1972 meeting of the Royal Society of Medicine, the first two double-blind controlled trials of phenelzine in the treatment of phobic anxiety states were reported. In the Maudsley and St. George's trial, patients suffering from severely incapacitating agoraphobia and social phobias were treated with phenelzine or placebo in a flexible dosage regime (20-90mg daily, mean 2.6tablets) for 2 months. Forty patients entered the trial and 32 completed it. The overall improvement as assessed by phobias, other symptoms, free floating anxiety, panic attacks and social ratings, indicated that phenelzine was superior to placebo. The second trial of phenelzine in agoraphobia and social phobias was carried out by Solyom at the All Memorial Institute in Montreal. Five groups of 10 patients were matched and randomly assigned to: (a) systematic desensitization; (b) aversion relief; (c) flooding, (d) phenelzine 15mg three times a day with brief psychotherapy for 3 months; and (e) placebo with brief psychotherapy. The percentage of improvement in the phenelzine treated patients was found to be 80-90% compared to 40-50% of the patients on placebo. 10 references.

206368 Tyrer, Peter. Institute of Psychiatry, London SE5 8AF, England **Are monoamine-oxidase inhibitors antidepressants?** Proceedings of the Royal Society of Medicine (London). 66(9):950-951, 1973.

At the December 12, 1972 meeting of the Royal Society of Medicine, the effectiveness of monoamine oxidase inhibitors (MAOIs) was evaluated in a report of a test of whether clinical factors were useful predictors of response to phenelzine in chronic agoraphobic and socially phobic patients. Prospectively matched pairs of patients in which each patient on phenelzine was matched using double-blind procedure with one taking placebo were used. When the responses of the individual matched pairs were compared, in only one pair did the patient on placebo fare better than the counterpart on phenelzine, and in those with phobia of under 10 years' duration all patients on phenelzine were helped appreciably. 10 references.

206834 Gaillard, J.-M.; Eisenring, J.-J.; Tissot, R. no address **/Cerebral and peripheral consumption of L-5-HTP by patients suffering from maniacal, depressive or psychotic symptoms./** Consommation cerebrale et peripherique de L-5-HTP chez les patients atteints de syndromes maniaques, depressifs ou psychotiques. Encephale (Paris). 62(5):395-407, 1973.

Cerebral and peripheral uptake of L-(5-hydroxytryptophan (L-5-HTP) in patients with maniac, depressive or psychotic syndromes was tested. Differences between this drug and L-dopa in alteration of indolamine metabolism are also recorded. Age, sex, and diagnosis of patients, and medication administered before, during and after the tests are documented. Blood samples and flurometry were used to measure the effects of the L-5-HTP and levels of plasma 5-HTP, 5-HT (serotonin) and urinary 5-HIAA (5-hydroxyindoleacetic acid). A control population under L-dopa treatment was likewise treated. Extensive tables and graphs of results are given. Arterial levels were found to be consistently higher than venous levels, indicating upper arm and cerebral consumption of the drug. Depressive patients had clearly higher values than did other patients under the same treatment. Consumption of L-5-HTP was not a simple function of arterial levels of amino acid. Doses of decarbosylase inhibitor (benserazide HCl) greatly increased the percentage excretion of 5-HTP. 21 references.

207532 Murphy, J. E.; Donald, J. F.; Molla, A. L. no address **Oxypertine in the treatment of morbid anxiety. Report of a new low dosage schedule.** Journal of Int. Medical Research. 1:573-579, 1973.

One hundred general patients were used in double-blind study to test two doses of oxypertine in anxiety treatments. The two doses used were 10mg and 5mg three times a day. In some patients, the larger dosage induced anxious agitation. Sensibility tests were run on patients. Clinical evaluation of patients was achieved using the modified Hamilton anxiety rating scale which was administered after 2 to 4 weeks of treatment. Meanwhile, patients measured their own progress with the nine item visual analog scale. After the 2-4 week treatment, most patients showed similar and significant improvement. Tolerance was high and there was only a slight incidence of side-effects. Since there was little difference in the effects of the two dosages, a dosage of 5mg, three times daily, was preferred.

209079 Bond, Alyson J.; James, D. Colin; Lader, Malcolm H. Institute of Psychiatry, De Crespigny, Denmark Hill, London, England **Sedative effects on physiological and psychological measures in anxious patients.** Psychological Medicine (London). 4(4):374-380, 1974.

Sedative effects on physiological and psychological measures in anxious patients were examined. Twenty outpatients with chronic anxiety states were tested on a battery of physiological and psychological tests after amylobarbitone sodium, chlordiazepoxide, diazepam, and medazepam or placebo. The benzodiazepines depressed slow wave and increased fast wave activity of the electroencephalogram, diminished the auditory evoked response, reduced fluctuations in the skin conductance and decreased motor speed on the Gibson Spiral Maze. Amylobarbitone had less physiological effect but impaired performance on the Gibson Maze and arithmetic tests. Significant correlations were found between the mean Hamilton and patient ratings and the physiological measures. It is concluded that physiological changes show useful correlations with clinical effects. 12 references. (Author abstract modified)

209080 Lader, Malcolm H.; Bond, Alyson J.; James, D. Colin. Institute of Psychiatry, De Crespigny, Denmark Hill, London **Clinical comparison of anxiolytic drug therapy.** Psychological Medicine (London). 4(4):381-387, 1974.

A clinical pharmacological investigation of the physiological, psychological and pharmacokinetic effects of benzodiazepines on 20 outpatients suffering from chronic anxiety states is reported. Each received five treatments: amylobarbitone sodium, chlordiazepoxide, diazepam, medazepam and placebo. Ss were assessed on the Hamilton rating scale and completed self-rating scales, composed of at least three prime symptoms chosen by the S and phrase in his own words, as well as loss of appetite and insomnia. Neither placebo nor amylbarbitone produced any substantial improvement from predrug levels of anxiety but all three benzodiazepines produced significant and very similar decreases in both Hamilton ratings and self-ratings of symptom severity. The two measures also correlated highly. The majority of the Ss continued with medazepam at the end of the formal trial. 11 references. (Author abstract modified)

209081 Robin, Ashley; Curry, Stephen H.; Whelpton, Robin. Runwell Hospital, Wickford, Essex, England **Clinical and biochemical comparison of clorazepate and diazepam.** Psychological Medicine (London). 4(4):388-392, 1974.

Clorazepate and diazepam were compared with respect to clinical effectiveness and concentrations of benzodiazepine compounds in plasma in 15 severely anxious outpatients. Each S was studied in a double-blind trial incorporating 2 week periods of the two drugs and of placebo. Psychopathology scores were highest at the end of the placebo periods and lowest at the end of the clorazepate periods regardless of the order of treatments. After diazepam, both diazepam and N-desmethyldiazepam were detected in blood and after clorazepate, only N-desmethyldiazepam was detected. N-desmethyldiazepam concentrations were higher after clorazepate. Clinical progress was apparently related to the concentration of N-desmethyldiazepam in plasma. 15 references. (Author abstract modified)

209411 Okuma, Teruo; Ogura, Chikara; Nakao, Takehisa; Kishimoto, Akira; Imai, Shiro; Nakazawa, Kazuyoshi; Oda, Noriko; Sunami, Yuzuru; Mamizu, Kazuaki. no address **A double-blind controlled comparison of bromazepam and diazepam.** Clinical Psychology (Tokyo). 15(7):753-769, 1973.

The therapeutic effect of bromazepam (BZP) and diazepam (DZP) on a population of 75 neurotic patients was evaluated over a 4 week treatment period. While DZP produced a greater improvement in symptoms as measured by a scale for neuroticism, BZP was superior to DZP in overall clinical evaluation made by psychiatrists. BZP was better than DZP in treating anxiety, tension, irritation, hypochondria, depression, neurasthenic state, and had a better effect on persistent complaints of subjective symptoms and attitude toward life. BZP was also more effective in treating recurrent neurosis. No significant difference in side-effects between the two drugs was noted. 8 references.

209412 Taneda, Masao; Murazaki, Mitsukuni; Oguchi, Toru; Sato, Kiichiro; Mochizuki, Yasunori; Hara, Toshio. no address **Clinical studies of D-40TA (triazolobenzodiazepine) -- crossover trial on sleep disturbances and sleep EEG in normal adults.** Clinical Psychiatry (Tokyo). 15(7):771-780, 1973.

The effects of the triazolobenzodiazepine derivative, D-40TA, on sleep disturbance and on normal sleep EEG were assessed. D-40TA and nitrazepam were shown equally effective in relieving neurotic insomnia. Electroencephalograms of normal Ss under D-40TA showed earlier onset of sleep and decreased Stage 1 sleep. The effect of D-40TA on stage 2 sleep was amibguous, but Stage 3 sleep increased in all Ss. Slow onset of REM period was observed but the length of REM period was unchanged. A regular alternate onset of Stage 2 and REM sleep after the initial REM onset was noted in all Ss. 13 references.

209485 Olgiati, Sandro G. 115 East Ninth Street, Apt. 19A, New York, NY 10003 **Clinical assessment of lorazepam in anxiety: a double-blind study.** Current Therapeutic Research. 17(1):13-22, 1975.

A double-blind study involving 63 adult outpatients suffering from moderate to severe neurotic anxiety is reported in which treatment with lorazepam in doses of approximately 3mg per day administered twice daily produced greater improvement of anxiety and associated symptoms than did placebo. Adverse experiences and changes in vital signs were not regarded as clinically significant. 11 references. (Author abstract)

209486 Rickels, Karl; Csanalosi, Irma; Gratch, Michael; Gingrich, Russell L., Jr.; Kelly, Edward A.; Mirman, Merrill J. Psychopharmacology Research Unit, Philadelphia General Hospital, Philadelphia, PA 19104 **Phenaglycodol in anxiety: a controlled study.** Current Therapeutic Research. 17(1):23-31, 1975.

A double-blind study of 163 outpatients (69 general practical patients and 94 unpaid symptomatic volunteers) was designed to compare the effects of phenaglycodol, chlordiazepoxide and placebo in anxious neurotic patients. Results support prior studies in finding no demonstrable significant treatment differences in favor of phenaglycodol over placebo. Phenaglycodol was also less effective than chlorodiazepoxide, suggesting that no clinical rationale exists for the use of phenaglycodol in anxiety. 8 references. (Author abstract modified)

209487 Deberdt, R. Psychiatrisch Centrum, Ieper, Belgium **Camazepam versus diazepam: a double-blind trial on psychoneurotic patients.** Current Therapeutic Research. 17(1):32-39, 1975.

Camazepam, a new benzodiazepine derivative, was compared with diazepam in a double-blind clinical trial on psychoneurotic outpatients. Patients were assessed by the Hamilton Rating Scale for anxiety. Camazepam was more effective than diazepam on anxious mood, intellect and general somatic symptoms. Camazepam was shown to be well tolerated and active on chronic anxiety and somatic symptoms. 7 references. (Author abstract)

209488 Carey, M. S.; Hawkinson, R.; Kornhaber, A.; Wellish, C. S. Medical Department, Ciba-Geigy, Summit, NJ **The use of clomipramine in phobic patients; preliminary research report.** Current Therapeutic Research. 17(1):107-110, 1975.

Therapeutic efficacy, tolerability and safety of clomipramine were studied in 20 patients with phobic neuroses. Assessments of progress were performed weekly using the Hamilton Depression Rating Scale and Phobia Rating Scale. Beneficial responses were achieved in 15 patients using total daily doses of 50mg to 150mg clomipramine. Most patients responded well to clomipramine, 50mg twice a day. Five patients were discontinued from therapy due to drowsiness, nausea and fatigue in the first 5 days of the study. These toxic effects may have stemmed from using too high a starting dose for this category of patients. 2 references. (Author abstract)

209489 Yaryura-Tobias, J. A.; Neziroglu, F. 1691 Northern Blvd., Manhasset, NY 11030 **The action of chlorimipramine in obsessive-compulsive neurosis: a pilot study.** Current Therapeutic Research. 17(1):111-116, 1975.

The action of chlorimipramine (G-34586) was studied in 12 obsessive-compulsive neurotic patients in a 4 week trial. Weekly results of the Obsessive-Compulsive Rating Scale indicated that the intensity of anxiety was reduced in all patients and obsessive-compulsive symptomatology in 57%. The results of the Hamilton Rating Scale showed significance at the 10% level. The Global Evaluation of therapeutic effect was of 86% in improvement of their symptomatology. Optimum dosage ranged between 50mg to 300mg daily. 5 references.

209795 Antonelli, F.; Cimica, M. no address **/Clinical experiments with "bromazepam" on psychoneurotic and psychosomatic patients with psychotherapy./** Sperimentazione clinica del "bromazepam" su pazienti psiconevrotici e psicosomatici in trattamento psicoterapico. Medicina Psicosomatica (Roma). 18(1):39-47, 1973.

Twenty patients with psychoneurotic or psychosomatic disorders, in addition to somatic disorders, were treated with bromazepam during psychotherapy. It was found that adminis-

tration of bromazepam facilitated improvement in clinical symptomatology, particularly with respect to psychic components. The administration of the compound facilitated the initiation or course of psychotherapy in 12 cases of the 20 studied, always by means of diminishing anxiety and tension, which permitted better contact with the patient. 12 references.

209904 Woodward, J. Arthur; Henry, B. W.; Overall, John E. Department of Psychiatry, University of Texas Medical Branch, Galveston, TX **Patterns of symptom change in anxious depressed outpatients treated with different drugs.** Diseases of the Nervous System. 36(3):125-129, 1975.

Patterns of drug treatment effects to determine different levels of symptom changes in 458 anxious, depressed subjects in a nonexperimental setting were studied. Thirteen commonly used psychotherapeutic drugs were compared for efficacy in producing change in symptoms of anxiety, depressive mood, and psychomotor activation level in this most common type of psychiatric clinic patient. The drugs were found to differ in relative effect on anxiety and depressive mood. Tranquilizers produced greater effect on depressive mood than anxiety, while the more sedative of the tricyclic antidepressants produced relatively greater effect on anxiety. Within each of the three major drug classes, the more sedative members of the class tended to have relatively greater effect on anxiety and the less sedative tended to have relatively greater effect on depressive mood components of the symptom picture. The results are viewed as being contrary to expectations. 20 references. (Author abstract modified)

210434 Fyro, B.; Beck-Friis, J.; Sjostrand, I.-G. Dept. of Psychiatry, St. Goran's Hospital, 112 81 Stockholm, Sweden **A comparision between diazepam and haloperidol in anxiety states.** Acta Psychiatrica Scandinavica (Kobenhavn). 50(6):586-595, 1974.

A double-blind crossover comparison of diazepam, haloperidol and placebo carried out in 51 outpatients with neurotic anxiety - tension states is reported. Each drug was given for 1 week and both were significantly better than placebo. Thirty three of the Ss had anxiety without obvious precipitating factors. In this group, diazepam was significantly better than haloperidol in eight of 15 items, but there was no difference with regard to subjective side-effects. Eighteen patients had anxiety resulting from recognizable factors. In this group, no significant difference in therapeutic effect was seen, although haloperidol gave fewer side-effects. 14 references. (Author abstract modified)

210506 Bozzoli, A. Universita degli Studi di Milano, Facolta di Medicina e Chirurgia, Milan, Italy **/Pharmacological treatment of phobic - obsessive psychoneuroses: psychodynamic and symptomatological aspects./** Trattamento farmacologico delle psiconevrosi fobico-ossessive: aspetti psicodinamici e sintomatologici. Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(4):804-836, 1973.

Psychodynamic and symptomatological aspects of treating phobic-obsessive neuroses with monochlorimipramine and chlopentixol were discussed. One of the major advantages offered by combined drug treatment and psychotherapy is the possibility of better managing the therapeutic effect with respect to the intensity and importance of the symptoms. The most favorable effects and best tolerance were obtained with doses of around 100mg of both drugs. Another advantage of using these two compounds was the synergism of action and the potentiating of therapeutic activity. Tolerance to both drugs was optimum, with no extrapyramidal effects. 34 references.

210684 Williams, James G. L.; Jones, John R.; Williams, Barbara. Nebraska Psychiatric Institute, 603 South 45 Street, Omaha, NB 68106 **The chemical control of preoperative anxiety.** Psychophysiology. 12(1):46-49, 1975.

The effect of a psychoactive chemical, diazepam, on reducing physiologically disruptive anxiety in young female patients about to undergo operation was investigated. In a double-blind study preoperative anxiety was measured by the Skin Conductance Anxiety Test (SCAT) after patients had been given either intravenous diazepam or placebo. It was found that diazepam reduced the SCAT scores of the more anxious patients to the level of the scores of the less anxious ones, while the latter's scores were not significantly changed. The validity of the SCAT as an objective measure of anxiety was again confirmed and it was concluded that not only did diazepam differenially reduce anxiety levels in accordance with the degree of axneity present, but that it also reduced to normal levels the excessive amount of thiopental sodium needed for the induction of anxious patients. 21 refernces. (Author abstract)

211344 Kawai, Haruo. National Nagoya Hospital, Japan **The effect of Alamon (hydroxyzine hydrochloride) and medazepam on neurosis tested by a double-blind method.** Medical Consultation and New Remedies (Tokyo). 11(7):163-174, 1974.

Twenty pairs of neurotic patients exhibiting anxiety, tension and depression were treated with Alamon (AL) or medazepam (MP) in a double-blind study. The results show that MP was effective in 13 patients and AL, in 10 patients. Side effects of MP included drowsiness, dizziness, dry mouth, and heavy stomach. Al induced dry mouth, drowsiness, blurred vision tremor and stomach trouble. MP was more effective in treating tension than AL; however, AL induced less dizziness than MP. 4 references.

211433 Capstick, Norman. Graylingwell Hospital, Chichester, Sussex, England **Clomipramine in the treatment of the true obsessional state: a report on four patients.** Psychosomatics. 16(1):21-25, 1975.

A preliminary report is made of an ongoing study of four patients suffering from obsessional symptoms who have been treated with the drug clomipramine (chlorimipramine; Anafranil). The therapy may be divided into three stages: the stage of increasing the dose to produce a satisfactory therapeutic effect; a maintenance stage; and a stage of reduction by a series of descending dose plateaus. The patients were treated on an outpatient basis. These cases indicate the effectiveness of clomipramine as an antiobsessional agent and for change in the life pattern and in personal attitudes. 5 references.

212163 Breulet, M.; Parent, M.; Bourdouxhe, Suzanne; Bobon, J. Clinique psychiatrique universitaire, Rue St. Laurent, 58, B-4000 Liege, Belgium **/Injectable Temesta, anxiety and anguish./** Temesta injectable, anxiete et angoisse. Acta Psychiatrica Belgica (Bruxelles). 74(3):278-293, 1974.

Intramuscular and intravenous lorazepam (Temesta) was tested on 28 hospitalized patients suffering psychic and/or sematic anxiety. The trial was open in 13 patients and a double-blind crossover in 15 patients. At 15mg/day, parenteral Temesta was significantly superior to placebo in treating acute and chronic manifestations of anxiety. Compared to diazepam, lorzepam was less hypnosedative. Side-effects other than insomnia of parenteral lorazepam were slight, and local and biological tolerance was slight. 16 references. (Journal abstract modified)

212166 Cloquette, R. Residence des Mottes 6, D-7503 Froyennes, Belgium **/Tentative double-blind treatment of anxiety with B 5833./** Essai de traitement de l'anxiete en double aveugle par le B 5833. Acta Psychiatrica Belgica (Bruxelles). 74(3):317-326, 1974.

In a double-blind test, the new benzodiazepine derivative B5833 was administered to 20 patients to test tolerance and effectiveness against anxious depressive psychoneuroses. Meanwhile, 20 other patients received placebos. Evaluation of therapy was made with The Clinical Global Rating Scale (CGRS) and Hamilton's Rating Scale for Depression (RSD). Statistical analysis of results was favorable to B5833. The drug was well tolerated and effective against anxious depressive psychoneuroses. 8 references. (Journal abstract modified)

212167 Lens, F. J. B. Nowelei, 13, B-1800 Vilvoorde, Belgium **/A new benzodiazepine, screened by a parallel double-blind test./** Une nouvelle benzodiazepine, passee au crible d'un test double aveugle parallele. Acta Psychiatrica Belgica (Bruxelles). 74(3):327-337, 1974.

In a double-blind clinical study, bromazepam was shown to be clinically superior to diazepam in psychoneuroses of various natures and more particularly in anxiety neuroses. A daily dosage of 7.5to 40mg gave 84% positive results; symptoms showed a favorable evolution with a satisfactory clinical tolerance. 7 references. (Journal abstract)

212179 Sizaret, P.; Degiovanni, A. Service de Psychiatrie "A", C.H.U., Tours, France **/Use of a benzodiazepine at high dosage levels: a statement on 50 observations./** Utilisation d'une benzodiazepine a doses elevees: bilan sur 50 observations. Information Psychiatrique (Paris). 50(8):881-886, 1974.

Tolerance of Tranxene, a benzodiazepine, was examined in a clinical study of 50 patients suffering from chronic severe anxiety. Tranxene was administered orally, in doses of 50-200mg/day for a period of a month to a year, either independently or in conjunction with thymoleptics or neuroleptics. The drug was well tolerated, even in cases of prolonged high dosage. Tolerance was dependent upon proper regulation of diet and restricted use in the aged. Psychological dependence was observed in some cases.

212490 Roelandts, A. no address **/Clinical study of an new antidepressant, melitracen, for 50 ambulatory patients./** Etude clinique d'un nouvel antidepressif original melitracen (Dixeran) chez 50 patients ambulatoires. Ars Medici (Nivelles) 28:49-59, 1973.

The results of treating 50 ambulatory patients with melitracen (Dixeran), a new antidepressant, are reported. Administration of 100-150mg/day of melitracen resulted in the following: 1) in 24 of the Ss melitracen had a good thymoanaleptic effect; 2) the majority of patients responded in less than a week; 3) no disinhibitory action was observed; 4) side-effects necessitated termination of treatment in 11 cases; and 5) therapeutic action was stable at a medium dosage range.

212938 Matsushita, Kesuke; Matsumoto, Kei. Department of Neuropsychiatry, Faculty of Medicine, Kagoshima University, Japan **Pathophysiological studies of manic-depressive psychoses: relationship between anxiety and excretion of urinary catecholamines.** Clinical Psychiatry (Tokyo). 15(11):1159-1165, 1973.

The relationship between anxiety and urinary excretion of catecholamines was studied in 11 patients with anxious depression who were treated with mecholyl (methacholine). Levels of urinary catecholamines and anxiety were measured before and after treatment. The level of urinary adrenalin and the stability of the excretion pattern were found to vary with the level of anxiety. A close relationship between urinary catecholamine excretion and autonomic function is suggested. 24 references.

213293 Kudo, Yoshio; Asai, Keiichi; Ueda, Koichiro; Ono, Tsuneyuki; Kameta, Hideaki; Kitajima, Shogo; Kimura, Yoei; Tanaka, Katsuyuki; Tsujio, Takehiko. Osaka Police Hospital, Japan **Double-blind examination of bromazepam (Ro5-3350) for the treatment of psychoneurosis.** Japanese Journal of Clinical Psychiatry (Tokyo). 2(4):515-524, 1973.

The effect of bromazepam on neurosis was studied, based on a double-blind experiment in which 32 neurotic patients were treated with bromazepam, 32 patients were treated with diazepam, and 31 patients were given placebo. According to psychiatrists' overall observation, bromazepam was effective in 78% of the patients; diazepam was effective in 73%; and placebo was effective in 44%. In the patients' subjective opinion, bromazepam was effective in 82%, diazepam in 80% and placebo in 46%. The symptom specificity of each form of treatment is discussed. Side-effects, such as drowziness, fatigue, dry mouth, impotence, articulatory disturbance, and nausea, were observed in 46% of those treated with bromazepam, 31% with diazepam and 19% with placebo. 3 references.

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

205606 Bambasova, E.; Bilkova, J.; Budinska, K. Psychiatric Hospital, 411 85 Horni Berkovice, Czechoslovakia **Papaverin in the treatment of geriatric patients.** Activitas Nervosa Superior (Praha). 16(3):192-193, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, reports two studies in which the effect of Papaverin was compared to oxyphylline. Thirty patients were followed, 15 men and 15 women aged between 52 and 93 years, most of them with the diagnosis of arteriosclerotic dementia. The pilot study group was neither subjected to any diagnostic choice, nor exposed to any scales. In the course of the continuous clinical assessment the papaverin group patients were more improved in comparison to their oxyphillin matches. The most frequently improved item was the decreases in anxiety and depression. Notable was an intellectual improvement and better verbal communication, social attitudes and behavior. Performance improved in some common everyday activities. The results seem to indicate that papaverin should be considered with more attention in relation to the therapy of geratric patients, especially in the therapy of arteriosclerotic dementia. 6 references.

205615 Nahunek, K.; Svestka, J.; Rodova, A.; Misurec, J. Psychiatric Clinic, Brno-Bohunice Jihlavska 102, Czechoslovakia **Further clinical and EEG experience with clozapine.** Activitas Nervosa Superior (Praha). 16(3):202-203, 1974.

At the 16th Annual Psychopharmacological Meeting, an investigation of the electroencephalogram (EEG) of 16 hospitalized patients (two women and 14 men, mean age 41.2years), before treatment and on the 10th and 20th day of clozapine therapy, was reported. The increase of slow alpha activity over the central part of the skull was also statistically significant and indicates the widening of the alpha focus over the frontal part of the skull. These changes are characteristic for the EEG neuroleptic syndrome. The marked increase in slow

activity which is regarded to be connected with the antipsychotic action was present in 13 patients. Good results were achieved in various syndromological schizophrenic as well as manic-depressive forms. In endogenous depressions and schizoaffective psychoses with depressive symptomatology and in patients with paranoid hallucinatory components a with amentilike elements, agitation and anxiety could be influenced. 2 references.

205637 Predescu, V.; Giurezu, T.; Tudorache, D.; Nica, St.; Ionescu, R.; Nicolschi, L.; Niturad, A.; Popovici, E.; Curelaru, S. Psychiatric Clinic, Buchurest, Rumania **Hydergine-thioridazine combination in the treatment of psychopathological states in old age.** Activitas Nervosa Superior (Praha). 16(3):237-238, 1974.

At the 16th Annual Psychopharmacological Meeting, a study of the use of a hydergine - thioridazine combination in the treatment of psychopathological states in old age was reported. The combination of hydergine and thioridazine proved to be useful for the remission or abatement of various mental disturbances developing on the background of a pathological senescence and brain atherosclerosis. This combination made possible the administration of small doses of thioridazine. 11 references.

205639 Novotny, V.; Kolibas, E.; Junasova, D. Psychiatric Clinic, Mickiewiczova 13, 801 00 Bratislava, Czechoslovakia **Our experience with the treatment of delirium tremens with diazepam.** Activas Nervosa Superior (Pragur). 16(3):240, 1974.

At the 16th Annual Psychopharmacological Meeting, an investigation of the use of the benzodiazepam derivatives in the treatment of alcoholic delirium tremens (AO) was reported. In the diazepam treated group the mean duration of psychotic symptoms was distinctly shorter. Somatic complications and exits were less frequent in the diazepam group. Psychiatric complications (unspecific dementia, Korsakov syndrome and Korsakov psychoses) were nonsignificantly more frequent. In the AD group treated with diazepam psychotic symptoms extincted within 48 hours in nearly 75%, in one third of cases within 24 hours after commencement of therapy. An early reduction of daytime doses of diazepam proved effective, at a premature reduction of night doses transitory deliriant syndromes may occur at night. The inverse relation the size of the dose and the incidence of somatic complication of AD was statistically significant. The comparison of diazepam with other tranquillizing drugs used in AD confirm the superiority of this compound.

207151 Couteaux, F.; Pinchard, A. Clinique Psychiatrique, Universite de Liege, Liege, Belgium /**Urgent chemical treatment of states of agitation.**/ Les traitements chimiques d'urgence des etats d'agitation. Revue Medicale de Liege (Liege). 29(13):391-394, 1974.

The six states of agitation most frequently dealt with in large general hospitals are discussed and methods of dealing with them are described. The diagnosis of such a state requires the elimination of the possibility of cranial trauma, hypoglycemic accidents, acute intoxication, and frontal tumoral troubles or disturbances. The six states of agitation discussed are excessive, acute mania, mental confusions and subconfusions, agitational states of which hallucinatory delirium was the main characteristic, anxious agitation, epilepsy and drunkeness. Six drugs are mentioned as treatments and immediant calmants: Dehydrobenzperidol, Haldol, Valium, Etumin, Dominal and Prazine, and Gardenal or Epanutin.

207271 Strogonov, Yu. A. no address /**On the use of sydnocarb for psychopharmacological correction of behavioral disorders of the cycloid type of accentuated personality in adolescents.**/ Primeneniye sidnokarba dlya korrektsii rasstroystv povedeniya u aktsentuirovannykh podrostkov tsikloidnogo tipa./ In: Lichko, A., Patologicheskiye narusheniya povedeniya u podrostkov. Leningrad, Ministerstvo zdravookhraneniya RSFSR, 1973. 105 p. (p. 55-60).

The effect of sydnocarb in correcting behavioral disorders was studied in adolescents with impaired adaptation mechanisms. All nine participating boys suffered from the cycloid type of accentuated personality from the age of 13, but had managed to keep it under control until the adjustment to college proved overwhelming. By the time they sought help at the age of 17 or 18, they had become apathetic and had lost faith in their mental capabilities. At this point, participants were subjected to sydnocarb doses of 5 to 10mg daily, and observed in an ambulatory state for 4 months. After several days, the adolescents became much more active, and their mental work capabilities were significantly increased. Emotional mood was not affected immediately, but only after an improvement in the adaptation mechanisms had already taken effect. 12 references.

207437 Eisdorfer, Carl. Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA 98195 **Observations of the psychopharmacology of the aged.** Journal of the American Geriatrics Society. 23(2):53-57, 1975.

Psychotropic drugs for use in the elderly are discussed under the descriptive categories of antipsychotic, antidepressive, antimanic, antianxiety, and cognitive acting. In the antipsychotic classification, special attention is given to side-effects and to dosage for the elderly. The section on cognitive acting drugs includes some pertinent observations on cognitive ability in the aging, the importance of correct diagnosis, and therapeutic strategy. The aged are a population at risk for not only disease, but iatrogenic illness due to direct and indirect drug action. Rational therapy involves understanding the underlying dynamics of the disease and thus the selection of the most effective treatment. Psychotropic drugs in an appropriate program are valuable therapeutic assets. 6 references. (Author abstract)

207580 Weiss, Gabrielle; Kruger, Elena; Danielson, Ursel; Elman, Meryl. Dept. of Psychiatry, Montreal Children's Hospital, 2300 Tupper St., Montreal, Quebec H3H 1P3, Canada **Effect of long-term treatment of hyperactive children with methylphenidate.** Canadian Medical Association Journal (Toronto). 112(2):159-165, 1975.

The effect of long-term treatment of hyperactive children with methylphenidate is reported. Three groups of hyperactive children were compared by various measures of outcome 5 years after initial evaluation: 24 were treated with methylphenidate for 3 to 5 years during the followup period, 22 were treated with chlorpromazine for 18 months to 5 years and 20 received no medication during the followup period. No statistically significant differences were found between the three groups on the following measures of outcome: emotional adjustment, delinquency, Wechsler Intelligence Scale for Children, Bender gestalt visual - motor test and academic performance. Initially there was a difference between the three groups on ratings of hyperactivity and family diagnosis. Hyperactivity scores decreased significantly over the 5 years; family diagnosis ratings changed little. It is felt that methylphenidate was helpful in making hyperactive children more manageable at home and at school but did not signifi-

cantly affect their outcome after 5 years of treatment. 23 references. (Author abstract modified)

207582 Minde, Klaus K. Dept. of Psychiatry, Hospital for Sick Children, Toronto, Ont., Canada **The hyperactive child.** Canadian Medical Association Journal (Toronto). 112(2):130-131, 1975.

The hyperactive child and his environment are discussed. In order to determine whether the child is hyperactive or is understimulated, the following steps should be taken: a complete physical history should be taken which includes behavioral symptoms at home and at school; children under the age of 5 years should receive stimulants only in exceptional circumstances; the maintenance dosage of any drug must be determined with caution; family counseling should be initiated; and above all, the child should be closely observed in his natural interaction with peers and with adults. Given correctly, the drug will help the hyperactive child to be able to use the relationships offered to him by his environment more effectively. 6 references.

207957 Shapiro, Arthur K.; Shapiro, Elaine. Payne-Whiteny Clinic, New York Hospital-Cornell University Medical College, New York, NY **Sexuality and Gilles de la Tourette's syndrome.** Medical Aspects of Human Sexuality. 9(2):100, 103-104, 109, 115, 120, 1975.

Gilles de la Tourette's syndrome and its connection with sexuality is discussed. Gilles de la Tourette's syndrome is characterized by involuntary movements, utterances, and occasionally by echo phenomena. It is noted that the use of foul language, or coprolalia, is the most disturbing symptom. Research findings which support a neurophysiologic explanation for the phenomena of coprolalia are reviewed. The effective use of haloperidol to control the symptoms of Tourette's syndrome is described, noting that a troublesome side-effect is the decrease in libido. Commentary by authorities in the field are provided. 10 references.

208571 Davis, John M. Illinois State Psychiatric Institute, University of Chicago School of Medicine, Chicago, IL **Psychopharmacology in the aged: use of psychotropic drugs in geriatric patients.** Journal of Geriatric Psychiatry. 7(2):145-159, 1974.

The effects of psychotropic drugs upon aged psychiatric patients ar discussed. With a few exceptions, both older and younger patients experienced the same therapeutic effects and side-effects. The elderly have more drug - drug interactions because they are likely to be taking medication for more than one ailment. Data are presented on drug - drug interactions, such as the interference of chlorpromazine with the hypotensive action of guanethidine, and the worsening that occasionally occurs when psychotropic agents such as the antiparkinsonian drugs, the phenothiazines, and the tricyclic antidepressants are combined. The latter interaction is shown to involve an atropine like psychosis resulting from the combined anticholinergic properties of the drugs. Atropine type toxicity was also observed in elderly patients. Lithium, antipsychotics, and antidepressants are recommended when indicated for the elderly. 30 references. (Author abstract modified)

208572 Lipsitt, Don R. Mount Auburn Hospital, Cambridge, MA **Psychopharmacology in the aged: discussion.** Journal of Geriatric Psychiatry. 7(2):160-164, 1974.

John Davis's article on psychotropic drug treatment of aged patient discussed. The need for prudence in the use of all pharmaceutical agents is underscored, particularly in geriatric patients. The tendency both to overuse and underuse drugs as part of the total treatment is noted. It is emphasized that, while elderly patients have more illnesses for which multiple drugs are prescribed, their drug taking habits are not always well supervised. Further research which will provide knowledge to foster judicious utilization of drugs is advocated. 3 references.

208573 Salzman, Carl; Shader, Richard I. Psychopharmacology Research Laboratory, Harvard Medical School, Massachusetts Mental Health Center, Boston, MA **Psychopharmacology in the aged: research considerations in geriatric psychopharmacology.** Journal of Geriatric Psychiatry. 7(2):165-184, 1974.

General research problems in evaluating drug effects within a geriatric population are outlined. Biologic, mental, or functional capacities beyond the age of 60 are seen to be heterogeneous, not homogeneous. Research problems in this age group include biologic variability, age, gender, dose, toxicity, polypharmacy, placebo effect, initial severity of symptoms, capacity to respond to drugs, and the unique problems of rating drug effect. Guidelines are suggested for drug research in elderly patients, which include thorough physical examinations, including peripheral blood screening and tests of cardiovascular and neurological functioning. It is emphasized that rating scales must reflect the greater heterogenity of this population. 46 references.

208574 Cole, Jonathan O. Department of Psychiatry, Temple University, Philadelphia, PA **Psychopharmacology in the aged: discussion.** Journal of Geriatric Psychiatry. 7(2):185-188, 1974.

Salzman and Shader's article on research problems in evaluating dru effects in a geriatric population is discussed. The importance of the population studied is stressed; a study of Alertonic in normal geriatric volunteers is cited, in which no difference was found between the drug and a placebo. A replication of Salzman's and Shader's study or a study repeated in more symptomatic patients is proposed. The possibility of using the EEG as a way of measuring biological versus chronological age is suggested. It is suggested that Salzman's and Shader's finding of acute sedation caused by diazepam may have resulted from administration of the drug during the day rather than at bedtime. Drugs like diazepam and the barbiturates are seen to have a possible double action, producing sedation and ataxia early and anxiety relief over a longer time period. The question of whether psychoactive drugs would be needed if the elderly were better treated by society is explored. It is concluded that drugs still would be needed to handle unavoidable sequelae in aging. 1 reference.

208575 Asnes, Daniel P. Geriatric Unit, McLean Hospital, Belmont, MA **Psychopharmacology in the aged: use of major psychotropic medications in treatment of the elderly: case examples.** Journal of Geriatric Psychiatry. 7(2):189-202, 1974.

Case histories are presented which illustrate a variety of reaction to psychotropic medications by inpatients on a psychiatric unit specializing in the care of middle-aged and elderly patients. Diagnostic categories discussed and psychotropic medications used in each case are as follows: depressive neurosis (thioridazine and amitriptyline); manic-depressive psychosis (chlorpromazine, benztropine mesylate, haloperidol, lithium carbonate); involutional paranoid state (chlorpromazine, trifluoperazine, benztropine mesylate, phenothiazine); chronic schizophrenia (chlorpromazine, dextroamphetamine, amitriptyline); and two cases of dementia

(chlorpromazine, thioridazine, haloperidol, benztropine mesylate). The conclusion is that medications aid the treatment of the mentally ill elderly, but that there is no exact psychopharmacological treatment for specific mental illnesses. It is suggested that effective doses of specific medications be found by applying clinical judgment to the progress of each individual case. 5 references.

208576 Savitsky, Elias. Kingsbridge Center, Jewish Home and Hospital for Aged, Bronx, NY **Psychopharmacology in the aged: discussion.** Journal of Geriatric Psychiatry. 7(2):203-207, 1974.

Daniel P. Asnes' article,, which presented case examples of the use major psychotropic medications in the treatment of the elderly, is discussed. The heterogeneous nature of the aged population is emphasized, not only in terms of existing individual differences, but also in terms of age as a significant variable. Brief comments are made on each of the cases. The patient's right to refuse treatment is discussed, and it is concluded that when patients are treated as individuals, both patient and therapist benefit.

208723 Sakamoto, Yoshio. no address **From hosptial treatment to community psychiatry -- second report -- outpatient emergency treatment of mental patients with the use of haloperidol.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(4):404-413, 1974.

The use of haloperidol in the emergency treatment of mental patient at an outpatient clinic is discussed. Specific case histories of a patient with chronic hallucinatory psychosis with delusions of persecution and of a schizophrenic with delusions of persecution and violent behavior are reported. Intramuscular injections of haloperidol and promethazine resulted in a quick reduction in abnormal behaviors. Treatment with haloperidol at the time of crisis has helped to avoid hospitalization and facilitates the socialization process. 7 references.

209019 Klapetek, Josef. Trida Osvobozeni 25/III, 77200 Olomouc, C.S.S.R. **/The antidepressive effect of Sandomigran./** Zur antidepressiven Wirkung von Sandomigran. Nervenarzt (Berlin). 45(4):213-214, 1974.

Antidepressive effects of Sandomigran on 80 migraine sufferers were studied. Twenty patients were divided into two groups and both groups, in a 4 weeks single-blind observation period, received a placebo. During the next 4 weeks one group received Sandomigran and the second group remained on the placebo. At the end of this period, Sandomigran had produced a significantly heightened mood. This change could be observed with statistical significance as early as 2 weeks after the beginning of treatment. Results substantiate the reported findings of earlier studies on the antidepressive effect of Sandomigran in migraine patients. 12 references. (Author abstract modified)

209044 Randazzo, S.; Guarnieri, B.; Corso, E. A.; Gargano, M. A. Clinica Dermatologica, Universita di Catania, Catania, Italy **/On the use of sulpiride with some skin diseases./** Sull'impiego della sulpiride in alcune dermatosi. Medicina Psicosomatica (Roma). 18(3-4):287-294, 1973.

Fifty eight patients suffering from dermatological disorders were treated with sulpiride. Fifty favorable results (24 improvements, 26 cures) and 8 failures were obtained. In the 18 patients with psoriasis, discrete improvement of the condition was revealed with attenuation of the erythemic - squamous component and reduction of the number of spots. In the cases of herpes simplex, protracted treatment with maintenance doses (100mg/day) resulted in an absence of relapse (even after 6 months) in 7 cases out of 10. Treatment with sulpiride revealed a marked modification of the neuropsychic component, improvement in humoral tone, decrease in anxiety, reestablishment of the waking - sleep rhythm and the affective - volitional sphere. 1 references.

209045 Comazzi, A.; Invernizzi, G.; Pruneri, C. Istitutio Clin. Psich., Universita di Milano, Milan **Variations in the autonomic nervous system after administration of dihydroergotamine in psychosomatic patients./** Variazioni del sistema nervoso vegetativo dopo somministrazione di diidroergotamina (DHE) in pazienti psicosomatici. Medicina Psicosomatica (Roma). 18(3-4):295-301, 1973.

Variations in the autonomic nervous system were investigated following administration of dihydroergotamine (DHE) to psychosomatic patients. No substantial behavioral differences were found among the various diagnostic groups (peptic ulcer, ulcerous colitis, asthma). No difference in response was found for the various forms of psychosomatic disorders. As for capillary pulse amplitude, the 10 patients who presented a regular base trace showed a response (vasoconstriction) qualitatively and quantitatively above that of normal controls. A decrease in the irregularity of the trace was also observed for respiration and cutaneous resistance. It is thus possible to isolate response modalities in psychosomatic patients which differentiate them from normal subjects by the reactivity profile of some neurovegetative parameters. 10 references.

209123 Filippini, C.; Galli, T. Istituto Psichiatrico Provinciale "Paolo Pini", Milan, Italy **/Reflections on the efficacy of new drug therapies on the occasion of using an original medication: sulpiride (Dogmatil)./** Considerazioni a proposito dell'efficacia delle nuove terapie farmacologiche in occasione dell'uso di un medicamento originale: il Sulpiride (Dogmatil). Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(2):356-371, 1973.

Psychopathological modifications observed in 20 patients treated with sulpiride (Dogmatil) for varying periods of time were discussed. The drug caused marked psychopathological changes in all the Ss treated. This new clinical picture can create behavioral problems in the patient, especially when there is a strong increase in anxiety; it is the expression of a profound change in in defensive mechanisms which allows reestablishing the mental state and frequent settling in less regressive positions. It is concluded that sulpiride is a drug which has considerable advantages with respect to therapeutic action. Side-effects are very rare or absent. 14 references. (Journal abstract modified)

209127 Itil, Turan M.; Wadud, Abdul. 150 White Plains Road, Tarrytown, NY 10591 **Treatment of human aggression with major tranquilizers, antidepressants, and newer psychotropic drugs.** Journal of Nervous and Mental Disease. 160(2):83-99, 1975.

Treatment of aggression with major tranquilizers (neuroleptics), antidepressants (thymoleptics) and some newer compounds is reviewed, and neuroleptics are observed to be frequently used antiaggression drugs despite significant differences in the pathogenesis of various aggressive disorders. If the aggression is associated with psychosis, chlorpromazine or haloperidol are the drugs of choice. Aggressive disorders within the acute and chronic brain syndromes are best treated with pericyazine, thioridazine, and thiothixene. For aggressive

symptoms of mentally retarded patients, especially those with epileptic syndromes, a new benzazepine (SCH-12,679) was found to be very effective. Aggression associated with alcoholism or narcotic addiction showed best responses to chlorpromazine and haloperidol. Major tranquilizers should be given cautiously to patients with clinically known epilepsy or abnormal electroencephalographic findings. 81 references. (Author abstract modified)

209128 Azcarate, Carlos L. Institute of Psychiatry and Human Behavior, University of Maryland School of Medicine, Baltimore, MD 21201 **Minor tranquilizers in the treatment of aggression.** Journal of Nervous and Mental Disease. 160(2):100-107, 1975.

Recent reports on animal studies and human clinical trials on the antiaggressive action of minor tranquilizers are reported, and discrepancies in findings are noted. Variables that could account for inconsistent findings and paradoxical reactions include dosage, acute versus chronic drug administration and possible qualitative differences among this group of agents. Individual variations as to presenting clinical picture, initial levels of anxiety and hostility and personality types are also mentioned. A study designed to test the efficacy of two benzodiazepines at dosages higher than those usually recommended is being carried out in a population of anxious, aggression prone individuals with poor impulse control. Preliminary findings indicate such doses have been well tolerated, and paradoxical rage has not been observed. 43 references. (Author abstract modified)

209129 Sheard, Michael H. Dept. of Psychiatry, Yale University School of Medicine, 34 Park St., New Haven, CT 06519 **Lithium in the treatment of aggression.** Journal of Nervous and Mental Disease. 160(2):108-118, 1975.

Behavioral and biochemical pharmacology of lithium and briefly reviewed, and the inhibitory role of lithium in several examples of animal aggressive behavior is noted. The use of lithium to control human aggressive behavior has resulted in controversial findings. Two studies are described in male prisoners with a major problem of hyperaggressiveness. Treatment with lithium resulted in fewer recorded reports for fighting. A study carried out with male delinquents also indicates that lithium effects an improvement in aggressiveness. Results are viewed with caution because these studies were either uncontrolled or single blind. 62 references. (Author abstract modified)

209130 Monroe, Russell R. Institute of Psychiatry and Human Behavior, University of Maryland School of Medicine, Baltimore, MD 21202 **Anticonvulsants in the treatment of aggression.** Journal of Nervous and Mental Disease. 160(2):119-126, 1975.

Evidence is presented which suggests that a circumscribed ictal phenomenon in the limbic system is responsible for aggressive behavior in individuals with episodic behavioral disorders, and the use of neuroleptics in treating these patients is discussed. Two studies are reported which suggest that chlordiazepoxide and/or primidone are effective in blocking activated abnormalities on the electroencephalograph and in effecting clinical improvement in many patients with repeated and frequent aggressive behavior. 4 references. (Author abstract modified)

209131 Blumer, Dietrich; Migeon, Claude. Dept. of Psychiatry, McLean Hospital, Belmont, MA 02118 **Hormone and hormonal agents in the treatment of aggression.** Journal of Nervous and Mental Disease. 160(2):127-137, 1975.

Evidence for the role of androgens in male aggressive and sexual behavior is reviewed, and the use of medroxyprogesterone acetate (MPA) in treating several groups of patients is reported. MPA has a marked antiandrogen property; it is effective in lowering the testosterone level and controlling certain otherwise intractable sex deviations. Findings in six patients treated for sex deviation are summarized, and effects of MPA in the treatment of 11 temporal lobe epileptics and five other patients with severe angry aggressive behavior disorders are reported. Most temporal lobe epileptics responded well to MPA. Weight gain and earlier sleep were consistent side effects. The values of plasma testosterone, serum luteinizing hormone and urinary 17-ketosteroids were decreased by the treatment. Four patients were XYY individuals with lack of control over their sexual aggressive or angry aggressive impulses. 20 references. (Author abstract modified)

209395 Ohara, Kenshiro; Kasahara, Hiroisa. no address **Application of lopramine (DB-2182) for the treatment of depressive state.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(1):97-105, 1974.

The effect of lopramine on depression was evaluated in 25 patients with neurotic depression, depressive disease, schizophrenia, and narcolepsy. The drug was somewhat effective in all but one patient and was extremely effective in 36%. The drug improved loss of volition, slow movement, inhibited thinking, depressive feeling, headache, and diurnal rhythm. Side-effects were observed in 16% of the sample and resulted in termination of treatment in only two cases. 5 references.

209399 Wako, Toshihisa; Fujii, Hiroo. no address **Physiological management of hospitalized psychiatric patients.** Japanese Journal of Clinical Psychiatry (Tokyo). 2(4):497-503, 1973.

Treatment of the physiological problems of hospitalized mental patients is considered. Hormone therapy has proven most effective on homeostatic disturbance in patients with circular psychosis and puerperal psychosis. Obesity in psychiatric patients is often accompanied by diencephalic - hypophysial disturbance which can be managed by exercise, dieting, and the termination of treatment with phenothiazines and butyrophenones. Liver function tests are also deemed important for patients under treatment with psychotropic medication. 10 references.

209702 Vaisanen, K.; Kainulainen, P.; Paavilainen, M. T.; Viukari, M. Central Institute of Vaalijala for the Mentally Retarded, 76940 Nenonpelto, Finland **Sulpiride versus chlorpromazine and placebo in the treatment of restless mentally subnormal patients -- a double-blind cross-over study.** Current Therapeutic Research. 17(2):202-205, 1975.

A controlled couble-blind crossover study with sulpiride, chlorpromazine and placebo was conducted on 60 restless oligophrenics resistant to previous drug therapy. Sulpiride effected a more positive behavior change, but only in the case of global assessment were results significant. Findings indicate that the beneficial effects of neuroleptics on the restlessness caused by brain dysfunction associated with mental retardation are very marginal. 4 references. (Author abstract modified)

209736 Quinn, Patricia O.; Rapoport, Judith L. Georgetown University School of Medicine, 3800 Reservoir Road, N.W., Washington, DC 20007 **One-year follow-up of hyperactive boys treated with imipramine or methylphenidate.** American Journal of Psychiatry. 132(3):241-245, 1975.

A 1 year followup of 76 hyperactive boys who had participated in a comparative study of methylphenidate, imipramine, and placebo is presented. It was found that there was a higher rate of discontinuance of imipramine than of methylphenidate in this sample and that both medications decreased the boys' rate of weight gain but had no significant effect on growth in height. This finding is of concern because larger doses than were used in this study are in use elsewhere. Teachers reported that the group of boys who had discontinued with medication showed continued hyperactivity and behavior problems in the classroom at 1 year. The two treatment groups showed continued improvement at 1 year in classroom and home behavior and did not differ significantly from each other. 18 references. (Journal abstract)

209750 Marshall, John R. Department of Psychiatry, University of Wisconsin, 427 Lorch Street, Madison, WI 53706 **The treatment of night terrors associated with the posttraumatic syndrome.** American Journal of Psychiatry. 132(3):293-295, 1975.

Three cases are described in which the frequency and intensity of night terrors associated with the posttraumatic syndrome were greatly lessened by administration of imipramine. In one case, the night terrors disappeared completely. Possible explanations for this effect of imipramine are discussed, including the drug's arousal preventing action. It is felt that the study of sleep electroencephalographs of patients suffering posttraumatic syndrome will prove helpful. 8 references. (Journal abstract modified)

209784 Faure, Henri; Faure-Martinet, M. L.; Boulin, J. Psychiatric Hospital, F 28800 Bonneval, France /**A year of investigations on 1035 MD in child and juvenile neuropsychiatry: clinical and EEG findings from 46 cases.**/ Un an d'etudes sur le 1035 MD en neuropsychiatrie infanto-juvenile: constatations cliniques et electroencephalographiques sur 46 cas./ Revue de Neuropsychiatrie Infantile etc. (Paris). 22(7-8):517-526, 1974.

A year of investigations of the drug 1035 MD with emotionally disturbed children and adolescents was reported. Eight cases of improvement out of 12 cases were found in the "profound mental retardation with serious behavior disturbances" classification; in the prepsychotic or psychotic organization category, 8 cases of improvement out of 13 occurred, of which 5 persisted after discontinuation of medication. In the "emotional disequilibrium or preneurotic and neurotic disturbances" classification, out of 21 observations, 17 cases of discrete, significant, or very remarkable improvement were observed. 1035 MD was also effective with epileptic patients. Electroencephalograms of the Ss were affected by the medication. Generally, 1035 MD removes inhibitions, improves social contacts, aids scholastic adaptation, and facilitates the psychotherapeutic relationship. It is suggested that the compound be more widely used in child neuropsychiatry.

210180 Nishida, Kohei; Namba, Tunehiko; Kato, Giichi; Nozawa, Akira; Saito, Toshiji; Tsutsui, Sueharu. 2nd Dept. of Internal Medicine, Toho University School of Medicine, Omori, Tokyo, Japan **A comparison of a new tranquilizer, sulpiride and oxazolam on psychosomatic diseases, neurosis and masked depression using double blind method.** Journal of the Medical Society of Toho University (Tokyo). 21(2/3):267-278, 1974.

Sulpiride and oxazolam were compared in a double-blind study of 44 clinic patients representing psychosomatic disorders, neurosis and masked depression. Capsules containing 50mg of sulpiride and 10mg of oxazolam were used in equivalent doses, and three to six capsules of each drug were administered daily for 3 weeks. Data for the 35 patients who completed treatment indicated that both drugs showed almost the same degree of efficacy and safety. 16 references. (Author abstract modified)

210211 Galetti, G.; Torriti, A. Ospedale Provinciale per Lungodegenti "Villa Serena", Monza, Italy /**The treatment of anxiety in the elderly with a new tranquilizer compound.**/ Il trattamento dell'ansia nell'anziano con un nuovo composto ad azione tranquillante. Giornale di Gerontologia (Firenze). 22(10):904-918, 1974.

The therapeutic effect of a minor tranquilizer (brofoxine) was investigated in 20 elderly patients with anxious depressive syndromes and disturbances in emotions, moods, and behavior. Brofoxine exhibited an effective anxiolytic effect in 80% of the cases treated. The drug was well tolerated at the doses established (0.61-1.25mg/kg/day); basal values of blood chemistry and clinical - instrumental parameters were unchanged, and no side-effects were observed. No interaction was observed when brofoxine was administered together with a number of other drugs (antibiotics, digitalis, hypotensive agents, vasodilators, antiparkinsonian compounds, diuretics, antidiabetic drugs, bronchodilators, polyvitamins, expectorants, etc.). 11 references. (Journal abstract modified)

210288 Ardizzone, E. C.; Busacca Dolleo, C. Universita di Messina, Cattedra di Psicologia del Magistero, Messina, Italy /**The passatization index of retardates treated with high doses of "GABA" and nucleotides.**/ L'indice di passatizzazione di subnormali trattati con forti dosi di "Gaba" e nucleotidi. Igiene Mentale (Trapani, Italy). 17(3):327-332, 1973.

The passatization index, introduced by Pisani and Nigro, was investigated in mental retardates treated with high doses of gamma-aminobutyric acid (GABA) and nucleotides. Treatment continued for 40 days; dosage was 90ml twice a day. Two electroencephalographic examinations were made at the beginning and end of treatment. The results obtained did not reveal significant changes due to the higher doses. 2 references.

210513 De Martino, G.; Giorgi-Conciato, M.; Gaudieri, V.; Caruso, D.; De Iorio, A. Ente Ospedaliero, Regionale Generale, O.O. R.R. di Napoli, XII Divisione Medicina Generale, 80100 Naples, Italy /**Treatment of psychosomatic gastrointestinal disorders in outpatients.**/ Trattamento dei disturbi gastrointestinali psicosomatici in pazienti ambulatoriali. Minerva Medica (Torino). 64(87):4583-4595, 1973.

Results obtained with Gefarnax in treating 42 outpatients with psychosomatic gastrointestinal disorders were reported. A marked reduction of subjective symptoms was observed at the end of treatment. The decrease was statistically significant and confirmed by a study of the distribution of patients into groups characterized by various degrees of severity. In addition, the following were observed: disappearance or marked improvement in radiological findings in 89% of the patients, and an increase in bodyweight, improvement of cenesthesia, reduction in asthenia, increased interest in usual activities, reduction in anxiety - depressive manifestations, and an improvement in interpersonal relationships. Gefarnax was effective in 90% of the cases without any appreciable difference in diagnostic groups. It was well tolerated. 27 references. (Journal abstract modified)

211202 Bocci, U.; Luzi, T.; Bignotti, N.; Toninelli, P. Ente Ospedaliero Generale di Zona-Asola, Mantua, Italy /**Considerations about the treatment of senescence.**/ Alcune con-

siderazioni sulla terapia della senescenza. Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(6):1302-1320, 1973.

Therapeutic and pharmaceutical limitations in the treatment of senility are discussed. Opinons of noted specialists on various drugs and vitamins such as Bl, PP, B6, B5, P and A, used in the treatment of senility, are listed. 52 references. (Author abstract modified)

211226 Fina, G.; Glielmi, N.; Mele, C.; Piazza, A. Ospedale Psichiatrico Provinciale "L. Bianchi", Naples, Italy **Clinical and psychometric evaluation of the action of vincamin in cerebral arteriosclerosis.** Valutazione clinica e psicometrica dell'azione della vincamina in arteriosclerotici cerebrali. Ospedale Psichiatrico (Napoli). 41(3):487-512, 1973.

Vincamin therapeutic activity is compared with a well known chemical compound based on alkaloid dehydrogenate derivatives of Secale Cornutum. Comparison is based on classical psychometric tests, manual skills and clinical observations. Vincamin appears to modify symptoms of affective instability and irritability, typical of cerebral circulatory insufficiency. Action appears analogous for cephal algia, vertigo and auricular troubles 55 references. (Author abstract modified)

211355 Egli, Meinard; Graf, Isabelle. Institut fur Elektroencephalographie der Universitat, Kantonsspital, Ramistrasse 100, CH-8006 Zurich, Switzerland **/The use of anticonvulsant treatment of behaviorally disturbed children with bioelectric epilepsy: a catamnestic study of 76 cases./** Uber den Nutzen einer antikonvulsiven Behandlung bei verhaltensgestorten Kindern mit bioelektrischer Epilepsie: eine katamnestische Studie uber 76 Falle. Acta Paedopsychiatrica (Basel). 41(2):54-69, 1975.

Seventy six patients with bioelectrical epilepsy were followed up over a mean period of 9.2years in order to examine the usefulness of anticonvulsant drugs. The results prove beyond a doubt that in such patients neither behavior disorders nor noncharacteristic seizure like manifestations respond to anticonvulsant drugs. The treatment of behavior disorders with neuroleptic drugs is recommended, and it is asserted that they may be given without fear of possible provocation of epileptic seizures. It is found that the sedative effect of many antiepileptic drugs is harmful in many cases, especially in children, where normally intelligent children are apt to show a considerable loss in the level of their performance in school. Seizures resulting from sudden deprivation of anticonvulsant drugs may occur and seem to confirm the diagnosis of clinically manifest epilepsy, leading to more intensive anticonvulsant therapy. The inconvenience of long-term treatment as well as the feeling of being labeled epileptic are further negative aspects of this type of prolonged therapy. 27 references. (Author abstract modified)

211365 Kaiya, Hisanobu; Kato, Hideaki. Department of Neuropsychiatry, Gifu University, Japan **Affects of L-dopa on the psychological symptoms of Pick's disease.** Clinical Psychiatry (Tokyo). 16(1):85-88, 1974.

The effects of L-dopa on the psychiatric symptoms of Pick disease, lobar atrophy of the brain, are examined based on experiences with a 61-year-old male Pick patient showing hypoactivity, anhedonia, impulsive behavior, and memory disturbance. The patient was treated with L-dopa in combination with vitamins and brain metabolic activators for 7 months. The patient became more talkative and less hypoactive and impulsive within 1 week of beginning therapy, but anhedonia and dementive symptomatology were unresponsive to treatment. Within 3 months of initiating therapy, the patient had completely relapsed. 14 references.

211434 Gross, Mortimer D. University of Illinois at the Medical Center, Chicago, IL 60612 **Caffeine in the treatment of children with minimal brain dysfunction or hyperkinetic syndrome.** Psychosomatics. 16(1):26-27, 1975.

An investigation was made of 25 children, diagnosed as hyperkinetic, comparing the effects of placebo, caffeine, methylphenidate (Ritalin), dextroamphetamine (Dexedrine), and imipramine (Tofranil, Presamine). Caffeine, at doses roughly equivalent to a cup of coffee morning and noon, did not help a single patient, and made most of them worse, as rated by mothers from their own observations combined with the reports of teachers. In contrast, the same patients were benefited, on the average, by methylphenidate, dextroamphetamine and imipramine. 10 references. (Author abstract)

211998 Schnetzler, J. P.; Alleon, A. M. Hopital Psychiatrique, 38120 Saint-Egreve, France **/Correction of autonomic effects of psychotropic drugs by large doses of dihydroergotamine in adults and the elderly./** La correction des effets vegetatifs des psychotropes par les fortes doses de dihydroergotamine chez les vieillards et les adultes. Information Psychiatrique (Paris). 50(7):779-781, 1974.

The efficacy of dihydroergotamine in correcting the orthostatic syndrome and troubles of an atropine variety was tested. Two groups of patients were chosen, one with a median age of 37, the other with a median age of 76. The first group received dosages between 150-300 drops, the second 120-200 drops. An analysis of the results led to the conclusions that high doses of dihydroergotamine were well tolerated; the symptoms disappeared in 80% of the cases and the only remaining symptom was constipation. 1 reference.

212241 Thorell, L.-H.; Wretmark, G. Department of Psychiatry, University of Linkoping, S-581 85 Linkoping, Sweden **A comparative study of N 7001 (Metrisil) and imipramine on a series of depressive patients.** Acta Psychiatrica Scandanavica (Kobenhavn). 50(5):508-515, 1974.

A statistical investigation open (28 patients) and double-blind (32 patients) trial confirmed the results of earlier trials which indicated that N 7001 (Metrisil) is as effective as imipramine in the treatment of depressive illness. The same number of patients improved in both series. In addition, it is of importance to note that five patients had to break off their treatment by imipramine due to a deteriorated mental status, while no such incident occurred among the patients treated by N 7001. Regarding N 7001, an improvement rated by the team after 8 days of treatment indicated a good final result, in contrast to imipramine. If the patient exhibits obvious neurotic traits, the outcome with N 7001 will be worse than if he does not. The same cannot be said of imipramine. It was also found that patients rated as inhibited showed a better outcome on N 7001 than those not inhibited. This difference between N 7001 and imipramine was, however, not quite significant on the 5% level. 2 references. (Author abstract modified)

212494 Debray, R.; Messerschmitt, P.; Lonchamp, D.; Herbault, M. no address **/The use of Pimozide in pedopsychiatry./** L'utilisation du Pimozide en pedo-psychiatrie. Nouvelle Presse (Paris). 2:2917-2918, 1973.

The use of Pimozide in pedopsychiatry is discussed. The experimental group of 187 children included 11 cases of infantile psychosis and 114 cases of disturbed social behavior. With a dosage of 2mg daily, 55% of the cases demonstrated improvement. There were 60% cures in enuresis and 75% improvement in troubles controlling sleep. Pimozide's antiaggressive activity is stressed.

212811 Juliano, Daniel B.; Gentile, J. Ronald. State University of New York, Buffalo, NY 14214 **Will the real hyperactive child please sit down? Problems of diagnosis and remediation.** Child Study Journal Monographs. No. 1-6:1-38, 1974.

The research literature on the symptomatology, etiology, performance and behavioral management of hyperactive children with normal intelligence is reviewed. Doubt is cast on the assumption of excessive total activity. The minimal brain damage hypothesis of etiology is concluded to be ambiguous, with little functional value or significance to educational remediation. Most of the drug treatment studies have been methodologically poor; it is argued that until specific biochemical deficits are demonstrated in hyperactives, which can be corrected by specific drugs, pharmacological treatments can best be considered adjuncts to other treatment programs. In this regard, behavior modification studies are reviewed and shown to have some promise in the treatment of hyperactives. A practical procedure is proposed for evaluating effects of treatments on hyperactive children in such natural settings as school or home. 188 references. (Author abstract modified)

213353 Nelson, Jere J. Doctor's Hospital, San Diego, CA **Relieving select symptoms of the elderly.** Geriatrics. 30(3):133-142, 1975.

The effect of Hydergine in relieving select symptoms of the elderly is discussed. The results of a comprehensive comparison of the efficacy of Hydergine and papaverine in achieving therapeutic goals for elderly patients with mild to severe symptoms are presented. Findings revealed favorable results with Hydergine in comparison with papaverine. The results indicate the potential of Hydergine as a significant therapeutic agent for the elderly people handicapped by such symptoms as dizziness, mood depression, and confusion. 14 references.

12 PSYCHOTOMIMETIC EVALUATION STUDIES

205766 Van Putten, Theodore; Hollingsworth, Charles E. UCLA-Brentwood Veterans Administration Hospital, Los Angeles, CA **Diphenylhydantoin in the treatment of LSD flashbacks: a case study.** Newsletter for Research in Mental Health, etc. 16(4):25-27, 1974.

A patient with severe LSD (lysergic acid diethylamide) induced "flashbacks" was treated with psychotherapy and trials of diphenylhydantoin and placebo under double-blind conditions. Results suggest that diphenylhydantoin is no better than placebo for the treatment of flashbacks. Improvement was attributed to psychotherapy and the meaning of medication. 8 references. (Author abstract)

205931 Bech, Per; Rafaelsen, Lise; Rafaelsen, Ole J. Psychochemistry Institute, Rigshospitalet, University of Copenhagen, Blegdamsvej, DK-2100, Copenhagen, Denmark **Cannabis: a psychopharmacological review.** Danish Medical Bulletin (Copenhagen). 21(3):106-120, 1974.

A psychopharmacological review of cannabis and delta1-tetrahydrocannabinol (THC) is presented, covering sources and chemistry; animal and human studies of pharmacokinetics, pharmacodynamics, and toxicology; and pharmacotherapy. THC is probably the predominant psychoactive component in cannabis (or a precursor of an active metabolite). Cannabis intoxication has specific characteristics, especially the increase in time and distance estimation. In high doses, cannabis and THC exert effects which cannot be distinguished from those of true hallucinogens such as LSD. It is, however, reasonable to place cannabis in a distinct category of its own due to the lack of cross-tolerance with hallucinogens, and the lack of (or very limited) development of tolerance. Brain damage or persisting psychic changes after prolonged cannabis use have not been proved at acceptable scientific standards, and these important problems are thus unsolved. Cannabis has its own distinct profile of action, and it is thus not possible to extrapolate from the effects of cannabis to the effects of other psychoactive substances, or vice versa. 108 references. (Author abstract modified)

206356 Moskowitz, Herbert; McGlothlin, William. Dept. of Psychology, University of Califronia, Los Angeles, CA 90024 **Effects of marihuana on auditory signal detection.** Psychopharmacologia (Berlin). 40(2):137-145, 1974.

Performance changes in auditory signal detection were examined for conditions of both concentrated and divided attention under four dose levels of marihuana. No differences were found between no treatment and placebo conditions, but significant dose dependent impairment of signal detection resulted for marihuana conditions under both concentrated and divided attention. Application of signal detection theory indicated that impaired performance was due to a decline in sensitivity, independent of changes in subject criteria. There was also some indication of change in criteria -- a greater tendency for erroneous reporting of a signal when it was not present. 13 references. (Author abstract modified)

206361 Harding, T. University Dept. of Psychiatry, Royal Edinburgh Hospital, Edinburgh, EH 10 SHF, Scotland **The effect of lysergic acid di-ethylamide on serum creatine kinase levels.** Psychopharmacologia (Berlin). 40(2):177-184, 1974.

Observations on serum creatine kinase levels are reported for seven patients following lysergic acid diethylamide (LSD) ingestion. All patients showed a transient rise in serum level, and this was greatest in those patients who became psychotic. 9 references. (Author abstract modified)

208593 Barfknecht, C. F.; Nichols, David E. Dept. of Medicinal Chemistry and National Products, College of Pharmacy, Univ. of Iowa, Iowa City, IA 52242 **Correlation of psychotomimetic activity of phenethylamines and amphetamines with 1-octanol-water partition coefficients.** Journal of Medicinal Chemistry. 18(2):208-210, 1975.

In an attempt to relate the hallucinogenic potencies in man of some biologically important amphetamines and phenethylamines, the l-octanol - water partition coefficients for 11 amphetamines were determined. Using these values and published Hansch pi constants, the log P for 17 additional amines was estimated. It was found that lipophilicity, as measured by the log of the partition coefficient, may be a significant detrminant of the level of hallucinogenic potency. Results suggest that an ideal log P value for psychotomimetic activity in man may be from 2.89 to 3.72. 5 references. (Author abstract modified)

211108 Fanciullacci, M.; Franchi, G.; Sicuteri, F. Dept. of Clinical Pharmacology, Headache Center, University of Florence, 85 Viale Morgagni, I-50134 Firenze, Italy **Hypersen-**

sitivity to lysergic acid diethylamide (LSD-25) and psilocybin in essential headache. Experientia (Basel). 30(12):1441-1443, 1974.

Sensitivity to lysergic acid diethylamide (LSD-25) and psilocybin was assessed in normal volunteers and patients with essential headache (EH) to determine if a deficiency of 5-hydroxytryptamine (5-HT) is responsible for migraine and other EH. Findings indicate a greater susceptility of the EH sufferers to nonhallucinogenic amounts of LSD-25 and psilocybin, which could be due to a particular blood-brain barrier permeability to these drugs, to a supersensitivity at the level of the central nervous receptors, or to both factors. 16 references.

211596 Hausner, Milan. Molakova 18, Prague 8 **The dynamic confrontation model as an integration of psychotherapy.** Psychotherapy and Psychosomatics (Basel). 24(4-6):497-499, 1974.

At the Ninth International Congress of Psychiatry held in Oslo, 1973, a paper was presented in which a dynamic confrontation model was proposed which seems to be applicable to every kind of integrative psychotherapy regardless of whether or not hallucinogenic drugs are used to alter the consciousness. Experiments which combine the theory and practice of experimental neurosis, brainwashing, and hypnosis with experience with the so called psychodysleptic psychotherapy (psycholytic and psychedelic sessions by means of hallucinogens) were discussed. 6 references.

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

205605 Zapletaiek, M.; Hubsch, T.; Zenata, L. Psychiatric Clinic, Hradec Karlove, Czechoslovakia **The effect of mefexamide on some autonomic and psychological tests.** Activitas Nervosa Superior (Praha). 16(3):191-192, 1974.

At the 16th Annual Psychopharmacological Meeting, a study of the effects of mefexamide on the autonomic nervous system and psychic functions were was reported. The drug has an effect on the autonomic nervous system in that it reduces the sympathicus tone. It is concluded that mefexamide mildly improve performance, vigilance and psychomotor speed and by reducing the tone of the sympathicus it stabilizes to a certain extent the autonomic nervous system which is desirable in the therapy of psychic disturbances. 4 references.

205621 Jovanovic, U. J. Department of Physiology and Pathophysiology of Sleep, Psychiatric Clinic, University of Wurzburg, Germany **Categories of psychotropic drug effects on sleep EEG and EOG.** Activitas Nervosa Superior Praha). 16(3):209-210, 1974.

At the 16th Annual Psychopharmacological Meeting, a system of psychotropic drug classification according to the effects on sleep electroencephalogram (EEG), sleep electrooculogram (EOG) and the phases of paradoxical sleep (PS) was proposed. The classification of the effects of psychopharmacological agents on sleep into 10 categoreis seeks to remedy incompleteness or inadequacies in previous attempts of classification in the following ways: it is based on a relatively high number of healthy subjects, aged 20-50 years; and in most cases 10-20 consecutive nights were recorded under the same laboratory conditions. The percentage of beta waves in the frontal region, latency time up to the first phase of paradoxical frequency of rapid eye movement (REM) sleep, duration of paradoxical sleep and the frequency of rapid eye movements were evaluated. 2 references.

205765 Houser, Vincent P.; Rothfeld, Benjamin; Varady, Alexander, Jr.; Burchard, Jean. Veterans Administration Hospital, Perry Point, MD **The effects of chronic phenothiazine treatment on adrenal-pituitary function in man.** Newsletter for Research in Mental Health, etc. 16(4):22-25, 1974.

The effects of chronic administration of phenothiazines upon the responsiveness of the adrenal - pituary axis were investigated. Ss were 10 chronic schizophrenics who had been receiving high doses of the phenothiazines for at least 2 months and 10 control subjects from the medical wards of a Veterans Administration Hospital. It is concluded that chronic treatment with phenothiazines does not reliably affect adrenal - pituitary function in man. The drug group did not differ significantly from the normal control group under any of the experimental conditions. Not only were baseline levels similar, but both groups reacted in an identical fashion when the adrenal - pituitary system was suppressed with dexamethasone or stimulated with adrenal corticotropic hormone. The only discrepancy occurred in response to dexamethasone where two subjects in the drug group showed elevated cortisol levels. These results strongly suggest that these two subjects may not have received their oral dose of dexamethasone. 6 references.

206057 Jalling, Birgitta. Department of Paediatrics, Karolinska Hospital, S-104 01 Stockholm 60, Sweden **Plasma and cerebrospinal fluid concentrations of phenobarbital in infants given single doses.** Developmental Medicine and Child Neurology (Tadworth, Surrey). 16(6):781-793, 1974.

Plasma phenobarbital concentration was followed after the administration of single doses orally in 19 cases and intramuscularly in 14, to 33 infants over 6 months of age. The doses were increased during the course of the investigation until plasma concentrations over 15mg/ml were achieved. The plasma phenobarbital half life varied between 37 and 133 hours. A correlation between the dose and the rate of disposition could be demonstrated; the higher the dose, the shorter the half life. The volume of distribution after intramuscular injection was 0.47 to 0.76 l/kg. In eight infants phenobarbital concentration in cerebrospinal fluid was determined. Equilibrium between plasma and cerebrospinal fluid seemed to be reached within 4 hours of administration of a single dose. 31 references. (Author abstract modified)

206058 Forsythe, W. I.; Redmond, A. Leeds General Infirmary, Great George Street, Leeds 1, England **Two controlled trials of tyramine in children with migraine.** Developmental Medicine and Child Neurology (Tadworth, Surrey). 16(6):794-799, 1974.

Two controlled trials of tyramine on children with migraine are reported. In the first trial of 59 children, headaches developed in 12 children after taking tyramine, in 10 after taking a placebo, and in four after ingestion of both tyramine and placebo. In the second trial of 38 children, five children developed headaches after taking tyramine, 11 after taking a placebo, and four after taking both tyramine and placebo. The results suggest that tyramine is not an important etiological factor in childhood migraine. A positive tyramine test, in its present form, appears to be of questionable value in childhood migraine, as it may be due to a spontaneous attack and not to the tyramine. 9 references. (Author abstract)

206788 Raaflaub, J.; Speiser-Courvoisier, J. F. Hoffman-La Roche & Co. AG, CH-4002, Basel, Switzerland /**On the pharmacokinetics of bromazepam in man.**/ Zur Pharmakokinetik von Bromazepam beim Menschen. Arzneimittel-Forschung (Aulendorf). 24(11):1841-1844, 1974.

The pharmacokinetic profile of bromazepam, a psychosedative drug, was determined in four adult men. After a phase of fairly rapid distribution, the drug is eliminated from the blood according to first order kinetics, and it obeys the rules of a one compartment model with reasonable accuracy. The half life of the elimination process is 20.5hours on an average. The mean value of the volume of distribution is 90% of bodyweight. The plasma levels after oral intake show that the drug is rapidly absorbed from the gastrointestinal tract. The peak levels are reached within 1-2 hours. The mean bioavailability of the orally given drug is 84%. In human blood plasma, 70.1% of bromazepam is bound to proteins; the drug is extensively metabolized, and the bulk of the metabolites are eliminated through the kidneys. The cumulative excretion of the total radioactivity in urine after intravenous injection of 14C-bromazepam attains plateau values in the range of 63.8% to 75.9% of the dose. 9 references. (Author abstract modified)

206806 Cameron, B. D.; Chasseaud, L. F.; Lewis, J. D.; Taylor, T. Dept. of Metabolic Studies, Huntingdon Research Centre, Huntingdon, England **The disposition of butriptyline in rats, dogs and man.** Arzneimittel-Forschung (Aulendorf). 24(1):93-96, 1974.

Comparative disposition of butriptyline, a new tricyclic antidepressant, is reported for rat, dog and man. Single oral doses of C-labelled butriptyline were readily absorbed by rats and dogs, and at least 90% of the dose was excreted within 3 days. Two human subjects excreted single oral doses more slowly, 57% and 78% respectively within 7 days. Variable plasma concentrations, and slow rates of excretion of radioactivity by man compared to animals suggested prolonged enterohepatic circulation of butriptyline metabolites. Plasma concentrations of butriptyline in dogs after oral administration were maximal after one hour and declined with a half life of 2.4hours, while little unchanged drug was present in human plasma after oral administration. Most of the urinary and plasma radioactivity in rats, dogs and man represented metabolites of butriptyline. Unchanged drug was extensively bound to the plasma proteins, but the metabolites were less bound. Species differences occurred in the biotransformation of butriptyline. 10 references. (Author abstract modified)

206941 Coleman, James H. Division of Clinical Pharmacy, University of Tennessee College of Pharmacy, Memphis, TN 38163 **Concepts in beta blockade.** Diseases of the Nervous System. 36(1):46-47, 1975.

Indications and contraindications for use of propranolol, a pharmacologically pure beta adrenergic blocking agent that acts by specific competition with an adrenergic stimulant for the beta-adrenergic receptors, reversibly blocking the receptor activating effect of the stimulant, are examined. It has traditionally been used for treating cardiac arrhythmias, pheochromocytoma, and idiopathic hypertrophic subaortic stenosis. Additional medical uses have recently been reported, including the treatment of alcohol and drug withdrawal symptoms. The contraindications and precautions attending its use should be carefully observed and its use should be monitored closely when administered in combination with other drugs. 6 references.

206974 Ackenheil, M.; Beckmann, H.; Hoffmann, G.; Markianos, E.; Nystrom, I.; Raese, J. Psychiatrische Klinik der Universitat Munchen, 8 Munchen 2, Nussbaumstr. 7, Germany **/The influence of clozapine on the excretion of MHPG, HVA, and 5-HIAA in urine and cerebrospinal fluid./** Einfluss von Clozapin auf die MHPG-, HVS- und 5-HIES-Ausscheidung im Urin und Liquor cerebrospinalis. Arzneimittel-Forschung (Aulendorf). 24(7):984-987, 1974.

A neurochemical study of clozapine, a new drug which effects marked improvement in acute psychotic patients without producing disturbances in extrapyramidal functions, is reported. Homovanillic acid (HVA) in cerebrospinal fluid is significantly increased and 3-methoxy-4-hydroxy-phenylglycol (MHPG) in cerebrospinal fluid is significantly decreased during treatment with clozapine. Only a slight increase of 5-hydroxyindoleacetic acid (5-HIAA) was found in cerebrospinal fluid. The serum dopamine-beta-hydroxylase activity was significantly reduced during treatment with clozapine. In urine, no changes in HVA and MHPG excretion were observed before or during treatment, but 5-HIAA was slightly increased. No correlation was found between MHPG levels in cerebrospinal fluid and urinary MHPG excretion. HVA and 5-HIAA also show no correlation. 23 references. (Author abstract modified)

206976 Breyer, Ursula. Institut fur Toxikologie der Universitat, 74 Tubingen, Wilhelmstr. 56, Germany **/Longitudinal studies on the metabolite pattern of perazine and related phenothiazines in humans and animals./** Langsschnittuntersuchungen uber das Metabolitenmuster von Perazin und verwandten Phenothiazinen bei Mensch und Tier. Arzneimittel-Forschung (Aulendorf). 24(7):989-990, 1974.

The time course of urinary excretion of metabolites of perazine was followed in eight patients during the first weeks of treatment and in two patients during ingestion and following abrupt withdrawal of the drug. Results suggest that there is an accumulation of desmethylperazine during the initial stage of treatment and a retarded elimination following its termination. Animals given repeated doses of perazine, prochlorperazine, perphenazine, trifluoperazine or fluphenazine accumulated N-dealkylated products in their tissues as well as metabolites resulting from partial degradation of the piperazine ring, to form an ethylenediamine structure. Further biotransformation leads to phenothiazinyl propylamine and its Cl and CF3 substituted derivatives, which are also formed, respectively, from promazine, chlorpromazine and triflupromazine. Continued excretion of phenothiazinyl propylamine sulfoxide by patients removed from perazine suggests an accumulation of ethylenediamine derivatives in humans. 8 references. (Author abstract modified)

206985 Beckmann, H.; Jones, C.; Goodwin, F. K. Section on Psychiatry, Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **/Different urinary excretions of 3-methyoxy-4-hydroxyphenylglycol and response to tricyclic antidepressive drugs./** Unterschiedliche Ausscheidung von 3-Methoxy-4-hydroxyphenylglycol im Urin und Ansprechen auf trizyklische Antidepressiva. Arzneimittel-Forschung (Aulendorf). 24(7):1010-1012, 1974.

Urinary excretions of 3-methoxy-4-hydroxyphenylglycol (MHPG) from a homogeneous series of 12 unipolar depressed patients were measured before and during the fourth week of treatment with either amitriptyline or imipramine. Imipramine subjects had low pretreatment urinary MHPG excretions, and amitriptyline subjects had high pretreatment MHPG excretions. These data suggest that an underlying disorder of norepinephrine metabolism might be present in some subtypes of depression. Serotonin disturbances may be responsible for other forms of depression. A rational basis for choosing between certain tricylic drugs in the treatment of depressive disorder could, if further confirmed, emerge from these findings. 26 references. (Author abstract modified)

206992 Petruch, F.; Schuppel, R. V. A. Neurologische Klinik, 74 Tubingen, Liebermeisterstr. 18-20, Germany /**Enhanced drug hydroxylation in man under diphenylhydantoin therapy.**/ Gesteigerte Hydroxylierung von Arzneimitteln beim Menschen unter Diphenylhydantoinbehandlung. Arzneimittel-Forschung (Aulendorf). 24(7):1023-1025, 1974.

The metabolic disposition of phenazone was studied in eight male epileptics before and after several months of treatment with diphenylhydantoin (DPH). The average half-life of phenazone fell from 10 hours in the first trial to 6.1hours after treatment. The quantity of phenazone excreted was unchanged in urine within 24 hours and decreased from 2.8% of the dose to 1.8% of the dose. The amount of 4-HO-phenazone, the main hydroxylated metabolite, excreted in the urine 24 hours after dosing increased from 18% to 29.5% of the dose during treatment with DPH. Similar results were obtained on the basis of creatinine output. These findings show an increased activity of hepatic microsomal drug hydroxylation which can be attributed to DPH. Determination of DPH blood levels suggests that there is no significant autoinduction of DPH. 16 references. (Author abstract modified)

207043 Viol, Geoffrey W.; Grof, Paul; Daigle, Lesley. Dept. of Medicine, St. Joseph's Hospital, Hamilton, Ontario, Canada **Renal tubular function in patients on long-term lithium therapy.** American Journal of Psychiatry. 132(1):68-70, 1975.

Ten patients with recurrent affective disorders who responded completely to long-term lithium therapy but who were otherwise unselected were tested for renal tubular concentrating and acidification ability. Findings indicate that, despite frequent symptoms of thirst, polyuria, and nocturia, all patients are able to concentrate urine normally and all show normal renal tubular acidification ability. Results reveal a significant correlation between erythrocyte lithium concentration and maximum urinary osmolality. 20 references. (Journal abstract modified)

207153 Geser, C. A.; Muller-Hess, R.; Dufresne, J. J.; Du-Buis, R.; Felber, J. P.; Vannotti, A. Departement de biochimie clinique, Clinique medicale universitaire, Hopital cantonal, CH-1011 Lausanne, Switzerland /**Effect of L-Dopa on pituitary hormones and on carbohydrate and fat metabolism in normals and in Parkinson's disease.**/ Utersuchungen uber die Wirkung von L-Dopa auf Hormone des Hypophysenvorderlappens und auf den Kohlenhydrat- und Fettstoffwechsel bei Normalpersonen und bei Morbus Parkinson. Schweizerische Medizinische Wochenschrift (Basel). 103(19):690-697, 1973.

The influence of various doses of levodopa on some growth hormones and fat and carbohydrate metabolism was investigated in 11 normal subjects and 14 patients with Parkinsonism. Blood glucose, fatty acids, free glycerol, cortisol, insulin, FSH and LH were measured after L-dopa and a control saline infusion was administered. It was discovered that insulin values did not differ in the two groups and that levodopa stimulated the secretion of pituitary hormone in healthy subjects. In patients with Parkisons's disease treated with L-dopa, the glucagon stimulated growth hormone release is significantly lower than in the same age control group. Three tables of plasma dosages and three graphs of these metabolic reactions per blood content are included. 40 references. (Author abstract modified)

207443 Beckmann, Helmut; Goodwin, Frederick K. Section on Psychiatry, LCS/NIMH, 9000 Rockville Pike, Bldg. 10, Rm. 4S-239, Bethesda, MD 20014 **Antidepressant response to tricyclics and urinary MHPG in unipolar patients: clinical response to imipramine or amitryptyline.** Archives of General Psychiatry. 32(1):17-21, 1975.

The possible relationship between predrug 3-methoxy-4-hydroxyphenylglycol (MHPG) excretion and antidepressant response was assessed by evaluating responders and non-responders by a strict rating critieria. Tricyclic treatment in urinary MHPG excretion and therapeutic response was also studied in this group of unipolar depressed subjects. It was discovered that the mean pretreatment MHPG was significantly lower in the nine responders using imipramine, but not those patients with amitriptyline. Treatment using either drug was associated with a significant decrease in MHPG excretion, which was independent of clinical response. Individual patient data is provided for 24 subjects in tabular form; responses per length of treatment are also depicted by the three graphs. 32 references. (Author abstract modified)

207444 Mendels, Joe; Stinnett, James L.; Burns, David; Frazer, Alan. Depression Research Unit, Department of Psychiatry, University of Pennsylvania, Philadelphia, PA **Amine precursors and depression.** Archives of General Psychiatry. 32(1):22-30, 1974.

The role of biogenic amines in the genesis of affective disorders and depressive illnesses was examined using fifteen patients. The amino acid precursors, levodopa and L-tryptophan were administered (double-blind) to subjects who had a clear-cut history of manic-depressive illness or recurrent depressive illness. Relatively large doses were not associated with sufficient clinical improvement to allow the patients to leave the hospital. It was concluded that no substantial improvement could be shown in ten of the 12 patients treated with either levodopa or L-typtophan. Side-effects and reactions according to the drug used, sex, age or severity of depression of the patient, and bipolarity of the illness were also measured. Results of previous experiments using these drugs and a precursor - load strategy are also summarized in tabular form. 118 references. (Author abstract modified)

209002 Hoffer, A. 1201 CN Towers, Saskatoon, Saskatchewan, Canada S7K 1J5 **Treatment of schizophrenia.** Journal of Orthomolecular Psychiatry (Regina). 3(4):280-290, 1974.

A broad spectrum approach to various schizophrenic syndromes is described which includes consideration of supernutrition and cerebral allergies. This approach is aided when necessary by temporary use of tranquilizers, antidepressants, antianxiety and other chemotherapeutic substances used by standard psychiatric practitioners. 31 references.

209350 Crammer, John. Institute of Psychiatry, Denmark Hill, London SE5, England **Lithium, calcium, and mental illness.** Lancet (London). No.7900: 215-216, 1975.

A marked decline in the urinary excretion of calcium in patients on lithium is reported. This reduced excretion comes on at the start of treatment, can persist as long as treatment continues and is reversed when treatment ends. This phenomenon has been seen in healthy volunteers and schizophrenics, as well as in manic-depressives. 2 references.

209789 Hucker, H. B.; Stauffer, S. C.; Clayton, F. G.; Nakra, B. R. S.; Gaind, R. Merck Institute for Therapeutic Research, West Point, PA 19486 **Plasma levels of a new pelletized form of amitriptyline for maintenance therapy.** Journal of Clinical Pharmacology. 15(2-3):168-172, 1975.

Plasma levels of amitryptyline and nortriptyline were measured in volunteers after 1 week of daily dosage with either 25mg twice daily of standard amitriptyline tablets or a single 75mg capsule of a new pelletized form of amitriptyline. Concentrations of both compounds were essentially equal at the end of 1 week's dosage with either dosage form, but were somewhat higher through the dosing time interval for the pelletized drug. 10 references. (Author abstract)

210089 Quidu, M.; Hillion, C.; Le Corre, A. Hopital Gourmelen, Quimper, France **/Heptaminol and tension disturbances induced by psychotropic drug therapy: clinical study./** L'Heptaminol et les perturbations tensionnelles induites par les therapeutiques psychotropes: etude clinique. Information Psychiatrique (Paris). 50(10):1053-1059, 1974.

The effects of heptaminol on low blood pressure induced by psychotropic drugs were examined. Two groups of patients were used: 1) 11 males with a long history of treatment with neuroleptics for chronic psychiatric disorders; 2) 16 recently hospitalized patients of both sexes with a history of short-term treatment with neuroleptics or tricyclic antidepressants. Arterial pressure was recorded every 2 days for several weeks and sample data are charted. Heptaminol was found to effect a rise in arterial pressure in Group 1. Those in Group 2 who had been treated with neuroleptics showed a complete remission of functional symptoms and those treated with antidepressants also showed an improvement after heptaminol treatment was instituted. Results show that treatment with neuroleptics or thymoanaleptics always affects the dynamics of circulation, and that these disturbances may exist even in absence of subjective complaints.

210209 Curran, Donald J.; Nagaswami, S.; Mohan, K. J. Menninger Foundation, Topeka, KS **Treatment of phenothiazine induced bulbar persistent dyskinesia with deanol acetamidobenzoate.** Diseases of the Nervous System. 36(2):71-73, 1975.

A case of bulbar persistent dyskinesia is presented in a patient who had been prescribed a phenothiazine derivative for 11 years. His symptoms improved with the use of deanol, which is thought to convert to acetylcholine after crossing the blood brain barrier. This improvement suggests that deanol may shift the neuroleptic induced dopaminergic - cholinergic system unbalance toward equilibrium by matching predominant dopaminergic effect or by enhancing deficient cholinergic action in the dopaminergic - cholinergic system. It is concluded that futher research in neuropharmacology is necessary to confirm this finding. 19 references. (Author abstract modified)

210221 Hine, B.; Friedman, E.; Torrelio, M.; Gershon, S. Department of Psychiatry, New York University School of Medicine, New York, NY 10016 **Morphine-dependent rats: blockade of precipitated abstinence by tetrahydrocannabinol.** Science. 187(4175):443-445, 1975.

To determine whether delta9-tetrahydrocannabinol (THC) could act antagonistically to the effects of morphine, male rats were implanted subcutaneously with a pellet containing 75 milligrams of morphine base or placebo, and naloxone hydrochloride (4 milligrams per kilogram of bodyweight) was administered 72 hrs later. Treatment with THC (2, 5, or 10 milligrams per kilogram) 1 hr before naloxone administration significantly reduced the intensity of abstinence: the two higher doses blocked the appearance of wet shakes and escapes, diarrhea, and increased defecation. THC did not induce abstinence itself, and prior treatment with cannabidiol was ineffective in reducing naloxone precipitated abstinence in animals with morphine pellets. Data suggest that THC may be of value in facilitating narcotic detoxification. 13 references. (Author abstract modified)

210276 Koshino, Yoshifumi; Otsuka, Ryosaku. Department of Neuropsychiatry, Kanazawa University, Kanazawa, Japan **Psychotropic drugs and electroencephalography: third report.** Clinical Electroencephalography (Osaka). 16(3):184-193, 1974.

The literature on the effect of psychotropic drugs on electroencephalograms (EEG) and the use of EEG studies in psychopharmacology is reviewed. The influence of lithium, mescaline and lysergic acid diethylamide (LSD-25) on human EEG, and the advantages of using the EEG to investigate effects of psychotropic drugs on central nervous system function, clinical effects of psychotropic drugs and to prevent side-effects of psychotropic drugs are considered. 54 references.

210419 Laborit, H. Laboratorie d'eutonologie, Hopital Boucicaut, 75730 Paris Cedex 15 **/Action and reaction: bio- and neurophysiological mechanisms./** Action et reaction: mechanismes bio et neuro-physiologiques. Agressologie (Paris). 15(5):303-322, 1974.

The neurophysiological level of fundamental behaviors is discussed, and the semantic content of terms such as emotions, drives, motivation, and the role of memory and learning processes in their elaboration is described. Based on laboratory experiments, it is shown that it is necessary to distinguish between the sympathetic (noradrenergic) reaction, activated by a system of behavioral inhibition and expectation, and the medullo-adrenal (adrenergic) reaction controlled by a behavioral activation system when speaking of a defense reaction. The central role of the neurotransmitters is discussed, and it is suggested that the effect of catecholamines and the nicotinic effect of acetylcholine seem to have a direct role in the control of synaptic activity. A brief summary of the biochemical and neurophysiological mechanisms of drugs acting upon behavior patterns is included. 93 references. (Journal abstract modified)

210829 Teutsch, Grete; Mahler, Donald L.; Brown, Colin R.; Forrest, William H., Jr.; James, Kenneth E.; Brown, Byron W. VA Hospital, Bronx, NY **Hypnotic efficacy of diphenhydramine, methapyrilene, and pentobarbital.** Clinical Pharmacology and Therapeutics. 17(2):195-201, 1975.

The antihistamines diphenhydramine and methapyrilene were compared with pentobarbital for hypnotic effect in two Veterans Administration Hospital populations using subjective response methods. In the first part of the study, 60mg and 180mg of pentobarbital were compared with 50mg and 150mg of diphenhydramine. A positive dose response relationship was obtained only for pentobarbital; neither dose of diphenhydramine was significantly different from 60mg of pentobarbital for any response variable. In the second part of the study, 100mg of pentobarbital, 50mg of diphenhydramine, and 50mg of methapyrilene were compared with placebo. One hundred mg of pentobarbital and 50mg of diphenhydramine were significantly different from placebo but 50mg of methapyrilene was not. 12 references. (Author abstract)

211064 Dreifuss, Fritz E.; Penry, J. Kiffin; Rose, Stephen W.; Kupferberg, Harvey J.; Dyken, Paul; Sato, S. National Institute of Neurological Diseases and Stroke, Bethesda, MD **Serum clonazepam concentrations in children with absence seizures.** Neurology. 25(3):255-258, 1975.

The effects of clonazepam, a chlorinated derivative of nitrazepam, administered to 10 children with absence seizures were studied. Serum concentrations were measured after 8 weeks of treatment, at steady state. Seizure frequency reports and the 12 hour telemetered electroencephalogram were studied before and after 8 weeks of treatment to determine the frequency and duration of generalized spike-wave paroxysms. Eight of the 10 patients showed a significant decrease in seizure frequency, with three experiencing no seizures at all. Six patients had side-effects, predominantly drowsiness and ataxia. This preliminary study shows clonazepam to be useful in the treatment of absence seizures in children and to merit further study. 17 references. (Author abstract modified)

211258 Klein, Robert H.; Salzman, Leonard F. School of Medicine and Dentistry, Rochester, NY 14620 **Paradoxical effects of caffeine.** Perceptual and Motor Skills. 40(1):126, 1975.

The effects of caffeine on vertex averaged evoked potentials (AEP) produced by stimuli of varying intensity were studied. AEP amplitudes to stimuli of low intensity (1000 cps, 60 db) were lower 2 hours after ingestion of 300mg caffeine than responses to the same stimuli under placebo conditions. Findings suggest that the transient depression in brain activity observed by Tecce and Cole (1974) as a result of amphetamine administration may be a phenomenon also observable with other stimulants, although the time at which this effect manifests itself may vary from drug to drug. Taken together, findings support the suggestion that psychopharmacological studies should include longitudinal investigations of the effects of drugs. It is apparently not tenable to assume that the predominant or typical effect of a drug is exerted uniformly over the course of its action. 2 references.

212164 Meurice, E.; Remy-Schmetz, J.; Denys, W. J.; Spruyt, L. Institut Psychiatrique Provincial, B-6688 Lierneux, Belgium **/Preliminary study of a beta-blocker (pindolol) in three schizophrenics and three nonpsychotic psychiatric patients: differential sensitivity in heartrate./** Essai preliminaire d'un beta-bloqueur (pindolol) chez trois schizophrenes et trois malades psychiatriques non psychotiques: difference de sensibilite de la frequence cardiaque. Acta Psychiatrica Belgica (Bruxelles). 74(3):294-304, 1974.

A beta-blocker (pindolol) was administered in a series of tests to three schizophrenics and three nonpsychotic psychiatric patients. In the preliminary clinical trial, pindolol was administered after 1 month neuroleptic withdrawal to three therapy resistant chronic schizophrenics. In all three patients, the drug had to be discontinued after 5 to 6 weeks, without having reached 20% drop in heartrate and without therapeutic results. The drug was then administered to a psychopathic patient, a phobic patient, and an antisocial personality whose tachycardia was rapidly abolished by pindolol. Possible significance of differences in sensitivity is discussed. 12 references. (Journal abstract modified)

212277 Rogliani, G.; Bilotta, M. Ospedale Psichiatric Provinciale "L. Bianchi", Naples, Italy **/Gamma-aminobutyric acid and cerebral metabolism (preventive note).**/ Acido gamma-amino-butirrico e metabolismo cerebrale (nota preventiva). Ospedale Psichiatrico (Napoli). 41(2):199-210, 1973.

The role of gamma-aminobutyric acid (GABA) in nervous system metabolism, the conditions in which the turnover rate of this amino acid can change, and the effects such variations may have on nerve synapses are discussed. GABA applied directly to the cerebral cortex of mammals provokes: modifications in cortical activity through the substitution of positive waves for negative superficial negative waves; abolition of superficial negative postsynaptic potentials, evoked by electrical stimulation, and their substitution with positive superficial potentials; suppression of the superficial negative component of the thalamic stimulation cortical response. GABA also provokes improvement in regaining consciousness in comatose states; facilitates the resolution of the results of thrombosis and cerebral hemorrhages; and improves the emotional state in Ss who present signs of retarded psychic development. 13 references. (Journal abstract modified)

212432 D'yakova, S. D.; Korolev, V. V.; Maslova, A. F.; Shashkova, I. A. Kafedera psikhiatrii Moskovskogo meditsinskogo instituta im. N. I. Pirogova, Moscow **/The level of blood neuromediators after the use of seduxen as an index of nervous system reactivity./** Uroven' neyromediatorov v krovi pri ispol'zovanii seduksena kak pokazatel' reaktivnosti nervnoy sistemy. Zhurnal nevropatologii i psikhiatrii imeni S. S. Korsakova (Moskva). 74(11):1717-1722, 1974.

The influence of seduxen on the metabolism of blood neuromediators of emotional and vegetative - somatic reactions was studied in 74 healthy subjects, aged 20 to 35. During the first 3 days of drug administration, nonspecific placebo effect reactions were noted. Gradual increase in doses from 0.05 to 0.30 mg/kg led to an increase in catecholamine and acetylcholine content in the peripheral blood. Subsequent dose increase of 0.40, 0.50 and 0.60 mg/kg did not increase the number of neuromediators. A reduction in seduxen doses from 0.60 to 0.20 mg primarily influenced the character of acetylcholine elimination. 27 references. (Journal abstract modified)

14 MECHANISM OF ACTION: BEHAVIORAL

205622 Seifertova, D.; Richter, M.; Vinar, O. Institute of Psychiatry, Prague 8, Bohnice, Czechoslovakia **Influence of some biographic factors on the therapeutic drug response.** Activitas Nervosa Superior Praha). 16(3):211-212, 1974.

At the 16th Annual Psychopharmacological Meeting, an investigation of the influence of some chi-square biographical factors on the outcome of 6 weeks' chlorpromazine treatment in 150 schizophrenic patients was reported. Only four chi-square values indicated that the relationship was statistically significant: women improved more in the item motor activity than men, patients with elementary education improved more in the item appearance than the better educated ones, patients working manually improved more in the item appearance than intellectuals, and patients with better prognosis improved more in the item aggressiveness. It is concluded that only the item appearance seems to respond differentially to chlorpromazine in relation to the social background of the patients. 10 references.

205623 Medek, A.; Navratil, J.; Hrbek, Jan; Macakova, J.; Siroka, A.; Krejci, Z. Institute of Higher Nervous Activity, Dr. S. Allende 3, Olomou, C.S.S.R. **Comparison of the effects of atropine and cannabis upon the fixed conditioned alimentary motor reflexes in cats affected by nicotine.** Activitas Nervosa Superior Praha). 16(3):215, 1974.

At the 16th Annual Psychopharmacological Meeting, the results of an investigation of the interaction of nicotine and cannabis, containing titrated amounts of delta9-tetrahydrocannabinol (THC) on fixed condition alimentary motor reflexes in cats were reported. The comparison of the experiment with application of altropine alone and nicotine alone showed that both drugs impaired all followup criteria markedly. The com-

bination of atropine and nicotine even deepened the impairing effect upon the performance, while the full effects of cannabis inhibited the negative influence of nicotine and the recall of the fixed conditioned alimentary motor reflexes was complete. 3 references.

205624 Komenda, S.; Hrbek, Jan; Navratil, J.; Medek, A.; Macakova, J.; Siroka, A. Department of Medical Physics, Medical Faculty, Palacky University, Olomouc, Czechoslovakia **Markov chain as a model of verbal learning.** Activitas Nervosa Superior Praha). 16(3):216, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, describes an experiment in which the effects of some drugs on verbal learning was examined. The subjects learned to associate concrete stimuli with some meaningless syllables. The stimuli were demonstrated serially and the associations learned by the anticipation method. The learning process was studied as a general Markov chain. The conditional probabilities of correct response became stationary (i.e. independent of the trial number) if the condition had taken into account the kind of the past responses in at least three to four trials. 1 reference.

205627 Slanska, J.; Plevova, J.; Benesova, O.; Tikal, K.; Hvizdosova, J. Institue of Pharmacology, Medical Faculty of Hygiene, Praha 10 Srobarova 50, 100 42, Czechoslovakia **Alteration of psychosomatic reactivity after a single therapeutic dose of pentobarbital in relation to the sex of probands.** Activitas Nervosa Superior Praha). 16(3):218-220, 1974.

At the 16th Annual Psychopharmacological Meeting, an investigation of the effects of a single administration of pentobarbital in the dose of 100mg in 134 medical students was reported. In the 90th minute after drug administration, pentobarbital induced a statistically significant ddecline of vigilancy and increase of fatigue in comparison to the placebo as well as to control groups. The tension (considered as irritation) was increased in both pentobarbital and control groups compared with the placebo group. Concerning sex differences, the increase of fatigue after pentobarbital was significantly more evident in women. It is conluded that pentobarbital given in the afternoon had a sedative effect in the first hours after administration and later even a hypnotic effect. 2 references.

205945 Bruscky, Sergio Barbosa; Caldeira, Marcio Versiani; Bueno, J. Romildo. Clinica Psiquiatrica, Universidade Federal do Rio de Janeiro, Av Venceslau Braz, 71, 20000 Rio de Janeiro, GB, Brazil **/Clinical trial with sulpiride./** Ensaio clinico com sulpiride. Arquivos de Neuro-Psiquiatria (Sao Paulo). 32(3):234-239, 1974.

Oral or intramuscular sulpiride was administered to 39 patients suffering from a variety of psychiatric conditions. The treatment lasted from 20 to 90 days, at 1200mg/day. Side-effects were minimal, and results show that the treatment was satisfactory for treating anxiety, reactive disjunction and certain types of delirious and hallucinatory states. 13 references. (Author abstract modified)

206143 Maletzky, Barry M. Department of Psychiatry and Neurology, U.S. Lyster Army Hospital, Fort Rucker, AL **d-Amphetamine and delinquency: hyperkinesis persisting?** Diseases of the Nervous System. 35(12):543-547, 1974.

The clinical efficacy of d-amphetamine for delinquent behavior in adolescents and the relationships between such delinquency and hyperactivity of childhood were explored using sequential analysis. Fourteen subject pairs of delinquent teenagers were examined, and a significant positive effect was documented for d-amphetamine as compared to placebo when both were added to an ongoing psychotherapeutic regimen. Tolerance, withdrawal, and euphoria were not associated with d-amphetamine's use in the experimental subjects. Parallels were drawn between d-amphetamine's effects in delinquent adolescents and hyperactive children; a reanalysis of the data demonstrated close links between a history or a presence of hyperactive traits and a clinical response to d-amphetamine. Difficulties in employing d-amphetamine in this age group are acknowledged and suggestions for further research are offered. 20 references. (Author abstract)

206360 Stern, J. A.; Bremer, D. A.; McClure, J. Dept. of Psychology, Behavior Research Lab, 1420 Gratton St., St. Louis, MO 63104 **Analysis of eye movements and blinks during reading: effects of valium.** Psychopharmacologia (Berlin). 40(2):171-175, 1974.

Computer analysis procedures were used to evaluate the effect of Valium on visual search activity during reading. Visual search activity was monitored in 17 undergraduates before and after a week long regimen of Valium or placebo. Although Valium had little or no subjectively recognizable effect on participants in the study, computer analyses of electrooculograms indicated significant changes in the Valium group. Administration of Valium resulted in an increase in frequency of long fixation pauses, a general increase in duration of fixations following a line shift, and a decrease in velocity of saccadic eye movements during line shifts. The specific changes identified were consistent with an overall decrease in material read in the second session in the Valium group 5 references. (Author abstract modified)

206362 Adams, R. G. Health Department, Vale Drive Clinic, Vale Drive, Barnet, Herts., England **Pre-sleep ingestion of two hypnotic drugs and subsequent performance.** Psychopharmacologia (Berlin). 40(2):185-190, 1974.

The effects of presleep ingestion of nitrazepam and butobarbitone on subsequent performance were examined. Twelve subjects attempted five 15 minute tasks in a balanced, latin square design. The high dose of each drug increased the time on task decline in a short-term memory task. Short-term memory did not show a definite time of day effect. Proofreading was superior in the morning, but concept identification was faster in the afternoons. Implications of these findings are briefly discussed. 14 references. (Author abstract modified)

206369 Dunleavy, D. L. F. Dept. of Psychiatry, General Hospital, Nottingham NG1 6HA, England **Mood and sleep changes with monoamine-oxidase inhibitors.** Proceedings of the Royal Society of Medicine (London). 66(9):951, 1973.

At the December 12, 1972 meeting of the Royal Society of Medicine a study of 22 depressed patients monitored in the Sleep Lab in Edinburgh was reported. Each performed a daily self-rating of mood on a visual analog scale, and there was a deliberately varied placebo period before phenelzine was prescribed in randomly decided, daily doses of 60, 75, or 90mg, the dose remaining constant for each patient. The results show that there was a clear cut dose - response relationship, total abolition of the signs of REM sleep occurring in 7-8 days with 75 and 90mg, and taking 15 days with 60mg. Earlier observations that when mood response to phenelzine begins, it does so in a temporal association with a profound neurophysiological change that takes up to 3 weeks to be accomplished after the commencement of the drug were confirmed. 1 reference.

206450 Johns, M. W.; Masterton, J. P. Department of Surgery, Monash University Medical School, Alfred Hospital, Prahran, Victoria 3181, Australia **Effect of flurazepam on sleep in the laboratory.** Pharmacology (Basel). 11(6):358-364, 1974.

The hypnotic drug flurazepam was given to six healthy young men in a blind study involving sleep on four consecutive nights in the laboratory. Continuous recordings to the EEG, EOG, and electrical resistance of palmar skin made throughout the night enabled sleep to be analyzed objectively in terms of the usual stages. Sleep on the third night, when flurazepam 15mg was taken, was compared with that on the second and fourth nights, when a placebo was taken. Flurazepam permitted sleep which was objectively better and subjectively as good as the best sleep without the drug. There was no inhibition either of REM sleep or of delta wave sleep as occurs with many other hypnotics. 19 references. (Author abstract)

206926 Rosin, Arnold J. Harzfield Hospital for Chronic Diseases, P.O. Box 48, Gedera, Israel **Clinical features, etiology and treatment of facial dyskinesias in the elderly.** Journal of the American Geriatrics Society. 22(11):495-500, 1974.

Clinical features, etiology, and treatment of facial dyskinesias and buccal lingual masticatory are described in a study of 16 cases, 15 of which were in old people. The etiology of dyskinesia is discussed in relation to excess dopamine effect, and it is proposed that a restoration of the dopamine - cholinergic balance (possibly by physostigmine) might result in diminution of the movements. Graded doses of haloperidol or reserpine, or even perphenazine, are suggested for effective therapy, when indicated. Other possible causes of dyskinesia cited include the following: cerebral arteriosclerosis, cerebrovascular accident, senile chorea, and a side-effect of brainstem operations. 20 references. (Author abstract modified)

206977 Schneider, E.; Ziegler, B.; Maxion, H.; Badawi, M. Abteilung fur Neurologie der Universitat, 6 Frankfurt/M., Schleusenweg 2-16, Germany **/Long-term and short-term effects of sulpiride on sleep EEG in man./** Kurz- und Langzeiteffekte von Sulpirid auf das Nachtschlaf-EEG des Menschen. Arzneimittel-Forschung (Aulendorf). 24(7):990-993, 1974.

Effects of sulpiride on sleep electroencephalogram (EEG) in man were investigated in 11 psychiatric patients. Sulpiride is an antipsychotic drug not related to known compounds with psychotropic effects. Administration of 200 to 400mg of sulpride effected a shortening of the time until sleep onset, a reduction of waking periods combined with an increase of other sleep stages, including rapid eye movement (REM) sleep. The amount of body movements, was not altered. After a 3 week administration of 300 to 600mg orally, a marked increase in deep synchronous sleep (stage four) was seen, while waking periods were slightly increased. The REM sleep was not affected. Whether the increase in stage four sleep is dependent on neurophysiological action of sulpiride itself or results from improvement of the psychosis has not been determined. 13 references. (Author abstract modified)

207000 van Lommel, R.; Baro, F.; Dom, R. no address **The influence of haloperidol and penfluridol on the learning capacity of the schizophrenic.** Arzneimittel-Forschung (Aulendorf). 24(7):1072-1074, 1974.

The influence of neuroleptics on learning in psychotics was assessed in two experiments. In a double-blind study involving 19 chronically psychotic patients, a placebo treated group gave significantly more false responses on a subtest of the McQuarrie test than a haloperidol group; in a star tracing task, only the haloperidol group showed significantly improved learning. In the second experiment, 48 patients were divided into four groups, and two haloperidol and two penfluridol treated groups were placed in either a spontaneous learning or a verbal instruction situation. Results of the Similarities Test demonstrated that only the instructed groups learn. No significant difference was found between patients on haloperidol and those on penfluridol. 7 references. (Author abstract modified)

207140 Battegay, R.; Abt, K.; Bogdan-Pataki, N.; Burger, H.; Spiegel, R. Psychiatrische Universitatspolyklinik, CH-4051 Basel, Petersgraben 1, Switzerland **/Comparative studies of verbal interactions in a group of healthy subjects under the influence of psychopharmacological agents: with special consideration of YG-19256, chlordiazepoxide and placebo./** Vergleichende Untersuchungen der verbalen Interaktionen in einer Gruppe von gesunden Probanden unter der Wirkung von Psychopharmaka: mit besonderer Berucksichtigung von YG 19-256, Chlordiazepoxid und Placebo. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie (Zurich). 114(2):339-350, 1974.

In a double-blind comparative study, 10mg chlordiazepoxide, 10mg YG-19256 and placebo were examined with respect to their effect on the verbal interactions of a group of six healthy male Ss. The evaluation showed that it was not possible to provoke enough aggressive interactions in the experiment. It was also impossible to observe and measure the sedative effect of the drugs examined. Chlordiazepoxide tended to influence all of the Ss verbal activities. The group model employed here for examining psychotropic drugs was not suitable since the behavior of group members was also dependent on factors such as the individual character of the members, the duration of the trial, the size of the room, and the intervals between sessions. These conditions are difficult to reproduce. A setting in which the observers could record the experiments from outside the room, through a one way mirror, is recommended. 15 references. (Journal abstract modified)

207285 Angrist, Burton; Sathananthan, Gregory; Wilk, Sherwin; Gershon, Samuel. Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016 **Amphetamine psychosis: behavioral and biochemical aspects.** Journal of Psychiatric Research (Oxford). 11:13-23, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the correlation of psychosis with dopaminergic events in the central nervous system was discussed. Behavioral aspects in hospitalized and experimentally induced cases were presented. The similarities and differences between amphetamine psychosis and schizophrenia were discussed. Hallucinations and delusions are prominent in both conditions; visual and olfactory hallucinations are more frequent in amphetamine psychosis than schizophrenia. Animal stereotypy was seen as constituting a valid animal model for amphetamine psychosis. Noradrenergic mechanisms seem less critical in psychotogenesis than dopaminergic events. Serotonergic and cholinergic mechanisms affect or may indirectly mediate responses considered specifically "dopaminergic". 20 references.

207286 Davis, John M. Illinois State Psychiatric Institute, Chicago, IL **A two factor theory of schizophrenia.** Journal of Psychiatric Research (Oxford). 11:25-29, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, experiments based on the dopamine theory of schizophrenia were reviewed to complement the studies of Angrist et al. Schizophrenia was activated in already psychotic patients with small amounts of intravenous drugs. Methylphenidate is more potent than either d-amphetamine or l-amphetamine in worsening psychosis. Physostigmine seems to effect the psychomotor symptoms of mania and depression to a greater extent than the cognitive systems. These patients become psychotic by a dose of methylphenidate which does not make normal patients psychotic. This indicates a susceptibility in the schizophrenic patient to psychomotor stimulants which would be consistent with the dopamine mechanism of action. A dopamine theory of schizophrenia is a very promising lead, but research should continue with caution. 8 references.

207579 Joseph, A. no address /**Amitriptyline and depressive structures (on 100 observations).**/ Amitriptyline et structures depressives (a propos de 100 observations). Marseilles, 1973. 80 p.

The effects of the drug amitriptyline on 100 selected subjects over a period of 8 years are reported. The drug was one of the most effective antidepressants studied and had a very high rate of cure. It was also easily tolerated and manipulable, and was for this reason frequently used for schizophrenics. The ethical questions of antidepressant drug therapy and the use of drugs as controllers of symptoms rather than as curers of the structure of the disease were considered.

207771 Swift, W. J.; Swift, E. W.; Arellano, Max. Langley Porter Neuropsychiatric Institute, San Francisco, CA **Haloperidol as a treatment for adult stuttering.** Comprehensive Psychiatry. 16(1):61-67, 1975.

The usefulness of haloperidol as a treatment for adult stuttering was examined in a double-blind placebo study. Of 19 Ss who appeared for the first distribution of medication, 11 had been randomly assigned to the placebo group, and eight to the haloperidol group. Stutterers treated with haloperidol generally showed a significant improvement when compared to stutterers treated with placebo. Two weeks following the cessation of all treatment, stutterers who had been taking haloperidol tended to have returned to baseline and no longer showed significant improvement. Several unanswered questions with regard to the results indicate the need for caution in treating stuttering with haloperidol alone. 17 references.

207775 Pillard, Richard C.; Fisher, Seymour. 80 East Concord Street, Boston, MA 02118 **Chlordiazepoxide and phenobarbital in a model anxiety-inducing situation.** Comprehensive Psychiatry. 16(1):97-101, 1975.

The effects of benzodiazepine tranquilizer on persons in an anxiety inducing situation (i.e.,outpatient dentistry) are evaluated in one of several related studies. This study aimed to: (1) determine whether chlordiazepoxide would reduce anxiety in patients undergoing a standard a standard dental procedure; (2) determine whether the anxiety reduction would be greater in patients predicted to be highly anxious during dental procedures as contrasted with those predicted to be minimally anxious; and (3) compare chlordiazepoxide and phenobarbital on criteria of anxiety reduction and the presence of side-effects such as sedation. Medication effects were detected, but high dental phobics did not appear especially sensitive to medication effects and seemed to experience more pain during the procedures. The activating effect of the chlordiazepoxide is noted. 6 references.

208920 Butter, H. J.; Lapierre, Y. D. Ottawa University, Ottawa, Ontario, Canada **The effect of methylphenidate on sensory perception and integration in hyperactive children.** International Pharmacopsychiatry (Basel). 9(4):235-244, 1974.

The perceptual deficiencies of hyperactive children and the improvement of these deficiencies during treatment with methylphenidate are elucidated. Using the Illinois Psycholinguistic Ability Scale, hyperactive children were found to be 18 to 24 months less mature compared with the normal group. This effect was particularly evident in the tactile and auditory modalities. The recognition of sensory stimuli was also impaired in the auditory and tactile modalities. The auditory modality alone was improved with methylphenidate. The recognition of successive stimuli was not improved with methylphenidate, but the recognition of simultaneous stimuli of several modalities was improved by the drug. Hyperactive children indicated a maturational lag which can be partly corrected by the administration of methylphenidate. 14 references. (Author abstract)

209260 Gupta, B. S. Dept. of Psychology, Guru Nanak University, Amritsar, India **The effects of stimulant and depressant drugs on verbal conditioning.** British Journal of Psychology (London). 64(4):553-557, 1973.

The effect of stimulant and depressant drugs, affecting primarily either the central nervous system (CNS) or the autonomic nervous system, on verbal conditioning was examined. The subjects were allocated to three levels of the extraversion dimension of personality. A 5 x 3 randomized block design was replicated 10 times using the sentence completion technique. The study supports the following conclusions: introverted subjects are more easily conditioned than extraverted subjects; dexedrine facilitates, and phenobarbitone and chlorpromazine inhibit, the conditioning process; dexedrine does not improve the conditioning level of introverted subjects; ephedrine does not affect the process of conditioning; and variability (standard deviation) tends to increase under the influence of drugs primarily affecting the CNS. 29 references. (Author abstract)

209527 Ancona, Leonardo; Saraceni, Carlo. Istituto di Psicologia della Facolta Medica dell'Universita Cattolica S. Cuore, Rome, Italy /**The disinhibiting effect of N(1-ethyl-2-pyrrolidinyl-methyl-2-methoxy-5-sulfamide-benzam mide (solpiride).**/ Lieffeto disinibente della N(1.etil-2.pirrolidinil-metil-2.metossi-5.sulfamido-benzamid de (sulpiride). I. Archivo di Psicologia Neurologia e Psichiatria (Milano). 34(3-4):409-418, 1973.

The disinhibiting effect of sulpiride was investigated by creating an inhibitory state through hypnosis, with respect to reading a list of words, and releasing it with sulpiride. The double-blind experiment involved: posthypnotic inhibition in reading some words and the immediate measurement of the phenomenon; the random administration of the drug and placebo; reinforcement of the inhibition after 3 days of treatment; and measurement of residual inhibition after 7 days of treatment. The posthypnotic suggestion of inhibition was carried out in the two groups of Ss in a statistically similar measure. The control group did not show a significant decrease in inhibition while the experimental group exhibited markedly significant decreases. The drug thus exhibited a destructive effect on the posthypnotic suggestion. 16 references. (Journal abstract modified)

209533 Delaunay, J.; Guibert, S. Service de psychotherapie, Centre Hospitalier La Rochelle, La Rochelle, France

/Sulpiride in ambulatory treatment of chronic psychotics./ Le Sulpiride dans le traitement ambulatoire des psychotiques chroniques. Information Psychiatrique (Lyon). 50(9):965-968, 1974.

Use of sulpiride in ambulatory treatment of chronic psychotics is analyzed. The sample population included 13 schizophrenics, three paranoics, and four cases of chronic psychotic depression The 16 women and four men were given doses between 150 and 1200mg during the treatment period of 3-4 months. The medication was well accepted by patients, with a minimum number of side-effects. The psychosis was stabilized and remained latent during the treatment period, particularly for delirium and hallucinations, and the syndrome of schizophrenia. It is concluded that sulpiride is an effective neuroleptic inhibitor.

209857 Antonelli, F.; Lavarda, A.; Malignaggi, S. Scuola Centrale dello Sport di Roma, Rome, Italy /**The effects of a new sedative (Lexotan) on reaction times and on attentive capacity of a group of atheletes.**/ Gli effetti di un nuovo sedativo (Lexotan) sui tempi di reazione e sulle capacita attentive di un gruppo di atleti. Medicina Psicosomatica (Roma). 19(2):189-196, 1974.

A double-blind, cross over experiment was performed on 40 athletes who repeated three psychotechnical tests (evaluation of visual and auditory reaction time, and the Toulouse-Pieron attention test) after 2 days of treatment with 1) Lexotan (6mg x 5); 2) Lexotan (3mg x 5); 3) Lexotan (1.5mg x 5); and 4) placebo. It was found that the administration of a single dose of Lexotan (bramazepam) a half hour before testing, in doses varying from 1.5mg-3mg, facilitates perception, slightly but certainly, and significantly increases attention. The practical consequences of this research offer the sports psychologist a harmless and valid pharmacological means of facilitating performance in cases where it may be compromised due to a state of anxiety. 9 references. (Author abstract modified)

209981 Borbely, A. A. Pharmakologisches Institut der Universitat, Gloriastrasse 32, CH-8006 Zurich, Switzerland /**The effects of hypnotic drugs on sleep.**/ Die Beeinflussung des Schlafes durch Schlafmittel. Schweizerische Medizinische Wochenschrift (Basel). 103(45):1585-1591, 1973.

The influence of some tranquilizing drugs on the various phases of natural and deep sleep in young adults and patients was studied in several experiments. Tables showing dosage of 11 hypnotic drugs and profiles indicating the number of hours of orthodoxical and paradoxical phases of sleep over a 3 or 4 night period have been complied. It is concluded that the mechanisms of action of hypnotics is still largely unknown. The electroencephographic record toxicity, aftereffects, and quality of sleep of the various pharmacological agents such as benzodiazepines, barbituarates, and alcohol are reported. The hypnotic action of various agents reducing the length of the deep stages of orthodox sleep is also considered. 55 references. (Journal abstract modified)

210088 Audisio, Michel; Membrey, Jean-Michel; Pisarz, Alain. Service de sante mentale de la Vallee de la Seine, 4, rue Paul-Eluard, 76301 Sotteville-les-Rouen, France /**Research on psychiatric indications of a powerful anxiolytic, lorazepam.** Recherceh sur les indications psychiatriques d'un anxiolytique puissant, le lorazepam. Information Psychiatrique (Paris). 50(10):1045-1052, 1974.

Lorazepam was tested for psychiatric effects on 62 patients grouped according to age, diagnosis, and duration of treatment. Ages ranged from 25 to over 75; doses were between 4 and 15 mg with most patients receiving 10 mg; treatment lasted up to 12 months. Lorazepam was well tolerated by the majority of patients. Its anxiolytic effect was strong, swift and lasting, and it was generally compatible with other psychotropic drugs. 17 references.

210210 Lion, John R.; Hill, James; Madden, Denis J. Institute of Psychiatry and Human Behavior, University of Maryland School of Medicine, Baltimore, MD 21201 **Lithium carbonate and aggression: a case report.** Diseases of the Nervous System. 36(2):97-98, 1975.

A case is presented which illustrates the effective use of lithium carbonate in treatment of a mentally retarded, aggressive young man prone to impulsive outbursts of a cyclical nature. Results suggest that, while the indications for lithium in the treatment of aggressive patients remain undetermined, the drug should be considered in the therapeutic armamentarium for selected violent patients. 15 references.

210286 Busacca Dolleo, G.; Salva, L. Universita di Messina, Cattedra di Psicologia del Magistero, Messina, Italy /**Changes in mental age with subnormal children treated with doses of "GABA" and nucleotides.**/ Modificazioni dell'eta mentale in subnormali trattati con forti dosi di "Gaba" e nucleotidi. Igiene Mentale (Trapani, Italy). 17(3):315-319, 1973.

The modifications in mental age in subnormal children treated with large doses of gamma-aminobutyric acid (GABA) and nucleotides were investigated in a double-blind study. The daily dose was 90ml, given in two administrations. Testing was done at the beginning of the experiment, after 15 days, on the 30th and 60th day. An examination of the results shows that improvement was evident especially in the first 15 days. Those treated went from a mental age of 9.8to one of 14.2; the children who were not treated only attained a mental age (MA) of 12.6. The subsequent increase was more modest. It is concluded that large doses have greater effectiveness. 1 reference.

210291 Ardizzone, E. C.; Busacca Dolleo, C. Universita di Messina, Cattedra di Psicologia del Magistero, Messina, Sicily /**Mnemonic capacity of mentally retarded boys treated with high doses of nucleotides and GABA.**/ Capacita mnemonica di subnormali trattati con forti dosi di nucleotidi e "Gaba". Igiene Mentale (Trapani, Italy). 17(3):343-345, 1973.

The mnemonic capacity of mentally retarded boys treated with large doses of nucleotides and gamma-aminobutyric acid (GABA) was investigated. Daily dosage consisted of 90ml, administered twice a day for 40 days. Two examinations were made, one at the beginning and one at the end of the experiment. The test consisted of electromyographic recording of flexor muscle electrical contractions during normal conditions, with "slow" music, and with "lively" music. The results seem to indicate a tendency toward an increase in the frequency of the points, but not toward a modification of the effect of the music. 3 references.

210293 Ardizzone, E. C.; Busacca Dolleo, C. Universita di Messina, Cattedra di Psicologia del Magistero, Messina, Italy /**Temporal discrimination tests in mental retardates treated with nucleotides and GABA in high doses.**/ Test di discriminazione temporale in subnormali trattati con nucleotidi e "Gaba" in forti dosi. Igiene Mentale (Trapani, Italy). 17(3):357-361, 1973.

Temporal discrimination was tested in mentally retarded boys treated with large doses of gamma-aminobutyric acid (GABA) and nucleotides. Daily dosage was 90ml; treatment lasted for 60 days, and examinations were made after 15, 30,

and 60 days from the beginning of the experiment. The drug had no effect on temporal discrimination. 2 references.

210296 Ardizzone, E. C.; Busacca Dolleo, C. Universita di Messina, Cattedra di Psicologia del Magistero, Messina, Italy **/The effects of nucleotides and GABA in large doses on the response to a painful stimulus with retardates./** Gli effetti di nucleotidi e "Gaba" in forti dosi sulla risposta allo stimolo dolorifico in subnormali. Igiene Mentale (Trapani, Italy). 17(3):375-379, 1973.

The effects of large doses of nucleotides and gamma-aminobutyric acid (GABA) on the response to a painful stimuli were investigated with mentally retarded boys. A daily dose of 90ml was administered at two times; treatment lasted for 40 days; and testing was done at the beginning and end of treatment. For the effect of repeating the painful sitmulus, the REC values decreased in controls and increased in treated Ss. This inversion of the results can be attributed to administration of the preparation. The number of rapid variations undergo a marked increase in the same conditions with treated Ss; the increase is moderate with controls. 2 references.

210418 Mangiameli, G. Cipollina. Via Gallia, 10, 00183 Rome, Italy **/Amenorrhea and behavioral disturbances: clinical case treated with a psychotherapeutic method based on elements of the cybernetic theory of G. Cipollina Mangiameli.** Amenorrea e disturbi comportamentali: caso clinico trattato con "Metodica psicoterapica su elementi di cultura cibernetica di G. Cipollina Mangiameli". Minerva Medica (Torino). 64(72):3765-3769, 1973.

A patient with amenorrhea and behavior disturbances caused by an obsessive anxiety neurosis and a depression syndrome is discussed. The amenorrhea was cured by a combination of psychotropic management with benzodiazepine and amitriptyline and a psychotherapeutic method based on cybernetics which requires independent activation of deconditioning. The neurotic, obsessive, phobic and behavioral disturbances also disappeared. It is felt that cryptogenetic syndromes might be explained by assuming that the synaptic activity of the cortex results in bioelectrical stimulation of the subcortical and endocrine structures. This stimulation would be paradoxical with respect to their normal function by triggering systematic reemergence of events conditioned according to Pavlov's laws concerning reflexes. 1 reference. (Journal abstract modified)

210530 Dantzer, Robert. Institut national de la Recherche agronomique, 180, chemin de Tournefeuille, 31300 Toulouse, France **/From psychopharmacology to psychopharmacogenetics: determinants of the effects of drugs on behavior, role of genetic factors./** De la psychopharmacologie a la psychopharmacogenetique: determinants des effets des drogues sur le comportement, role des facteurs genetiques. Annee Psychologique (Paris). 74(2):507-532, 1974.

Determinants of drug effects on behavior were studied through classification, with specific emphasis on the role of genetic factors. A brief explanation of behavioral tests and their analytical results is related to a developed schema of the behavioral action of drugs on the subjects. Principal categories of the psychotropic drugs are described and a general schema is developed from behavioral pharmacology. The action of drugs on the avoidance response is characterized, using chlorpromazine as an example. The difficulty of the task, motivation, mechanisms of suppression of avoidance and the effects of the drugs on acquisition and on extinction were all examined, and are used to examine the intervention of genetic factors. It is concluded that psychopharmacogenetic research must be carried out on two levels, the pharmacogenetic and the pharmacodynamic. 61 references.

210559 Namiki, Masayoshi; Kawakami, Kiyoshi; Hasegawa, Naoyoshi; Suzuki, Zinichi; Higuchi, Masamoto; Ueno, Kiyomitsu; Nakano, Shigeyuki; Tanaka, Masatoshi. Third Department of Internal Medicine, Hokkaido University School of Medicine, Japan **A double-blind controlled study of the thienodiazepine derivative (Y-6047) on neurotics and psychosomatic disorders.** Journal of Japanese Psychosomatic Society (Tokyo). 14(4):230-244, 1974.

A double-blind controlled study was conducted to evaluate clinical efficacy and safety of a new thienodiazepine derivative on patients with neuroses and psychosomatic disorders. A sample of 138 patients were randomly divided into three groups: 47 were administered Y-6047 as an experimental drug, 48 took diazepam and 45 controls took a placebo. Percentages of patients with excellent and moderate improvement in global judgment were 56% for Y-6047 group, 53% for diazepam group and 42% for placebo group. Main target symptoms of Y-6046 were anxiety, tension, irritability, insomnia, depressive mood, fatiguability, palpitation and poor appetite. Side-effects were dizziness and drowsiness in the Y-6047 group and in the diazepam group; dizziness, drowsiness and shakiness were observed in the placebo group. No abnormal laboratory findings caused by or related to the drug were reported. 3 references. (Author abstract modified)

210602 Gillin, J. Christian; Post, R. M.; Wyatt, Richard J.; Goodwin, Frederick K.; Snyder, Frederick; Bunney, William E., Jr. Laboratory of Clinical Psychopharmacology, NIMH, 10/3N222, Bethesda, MD 20014 **REM inhibitory effect of L-Dopa infusion during human sleep.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 35(2):181-186, 1973.

To determine whether L-Dopa has an inhibitory effect on rapid eye movement (REM) human sleep, 25mg to 50mg of the drug was infused to 10 depressed psychiatric patients pretreated with a peripheral decarboxylase inhibitor (MK-485 or MK-486). Pre-REM infusions of L-Dopa delayed the onset of REM sleep while infusions at REM onset shortened the length of the REM period. These data are consistent with the hypothesis that catecholamines suppress REM. 32 references. (Author abstract modified)

210680 Bartol, Curt R. Department of Psychology, Castleton State College, Castleton, VT 05735 **The effects of chlorpromazine and dextroamphetamine sulfate on the visual stimulation preference of extraverts and introverts.** Psychophysiology. 12(1):25-29, 1975.

The hypothesis that preference for visual stimulation is at least in part determined by physiological mechanisms which can be modified by depressant and stimulant drugs was assessed. Thirty six undergraduate females representing stable extraverts and stable introverts were used under diversive and specific exploration paradigms. While the specific exploration paradigm failed to reveal drug effects, the diversive exploration paradigm revealed that preference patterns of introverts were influenced by chlorpromazine, while dextroamphetamine sulfate had no significant effect on the preference patterns of extraverts. 25 refernces. (Author abstract modified)

210738 Pillard, Richard C.; McNair, Douglas M.; Fisher, Seymour. Psychopharmacology Laboratories, Division of Psychiatry, Boston University Medical School, Boston, MA 02118 **Does marijuana enhance experimentally induced anxiety?** Psychopharmacologia (Berlin). 40(3):205-210, 1974.

The question of whether laboratory stressors induce greater or more variable anxiety in marihuana intoxicated subjects was examined. In experiment 1, marihuana and placebo subjects were shown a motion picture film depicting dental procedures. In experiment 2, they were subjected to the stress of giving a short videotaped speech. No significant difference between marihuana and placebo subjects in anxiety response to these two stressors, as measured by a mood adjective rating scale, were found 7 references. (Author abstract)

210808 Saletu, B.; Allen, M.; Itil, T. M. Missouri Institute of Psychiatry, 5400 Arsenal St., St. Louis, MO 63139 **The effect of coca-cola, caffeine, antidepressants and C chlorpromazine on objective and subjective sleep parameters.** Pharmakopsychiatrie Neuro Psychopharmakologie (Stuttgart). 7(6):307-321, 1974.

The effects of coca-cola and a caffein sugar color matched beverage, as well as of tricyclic antidepressants and cholorpromazine, on the allnight sleep process of normal subjects were investigated as compared with placebo. Digital computer sleep prints showed that chlorpromazine increased deep sleep stages and rapid eye movement (REM) activity, while tricyclic antidepressants also augmented deep sleep stages, but attenuated REM activity and light sleep. Coca-cola and the caffein sugar beverage did not significantly influence the sleep profile. Computer period analysis of electroencephalogram (EEG) measurements obtained during total sleep and REM time demonstrated an increase of slow waves and decrease of alpha and slow beta activity after chlorpromazine and amitriptyline, while coca-cola and the caffeine sugar beverage attenuated fast activity. There were no significant differences in sleep latency and awakening threshold between the tested substances. The morning awake EEG was characterized after chlorpromazine by an increase of slow waves and decrease of alpha and slow beta activity, after amitriptyline by a concomitant increase of delta, theta, and beta activity and a decrease of alpha waves, while after the other substances no significant alterations occurred. 49 references. (Author abstract modified)

210871 Kiplinger, G. F.; Sokol, G.; Rodda, B. E. Lilly Laboratory for Clinical Research, Marion County General Hospital, Indianapolis, IN 46202 **Effect of combined alcohol and propoxyphene on human performance.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 212(1):175-180, 1974.

The effects of propoxyphene hydrochloride and ethanol administered alone and in combination to human subjects were examined. Placebo controls were used along with double-blind techniques. Performance was evaluated using tests for motor coordination, mental performance and stability of stance. It was found that a dose of 65mg of propoxyphene hydrochloride was associated with less impairment than was seen with ethanol alone in a dose producing a blood concentration of 0.05%. The effect of the combination was additive, with the ethanol effect predominanting. There was no evidence of potentiation of one drug by the other. 11 references. (Author abstract)

210879 Stitzer, M.; Domino, E. F. Worcester Foundation for Experimental Biology, 222 Maple Avenue, Shrewsbury, MA 01545 **Effects of d-amphetamine and secobarbital on key press rates in normal humans.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 207(2):288-297, 1974.

The effects of oral d-amphetamine and dl-amphetamine (0.2mg/kg) and secobarbital (2 and 3mg/kg) were studied on keypress responding in eight normal volunteers. Three rates of responding were generated with instructions and money as reinforcement in a three component multiple schedule. Rates were 2.1-14.6(component 1), 29.3-49.9(component 2) and 100.6-505 (component 3) responses/min. Pattern of responding within the min was either steady responding or a pause after reinforcement followed by a burst of responses. Secobarbital consistently decreased high response rates in component three in five out of eight subjects, but had no effect on lower response rates. Amphetamine in the dose given had no reliable effect on performance. 11 references. (Author abstract)

211070 Haffner, J. F. W.; Morland, J.; Setekleiv, J.; Stromsaether, C. E; Danielsen, A.; Frivik, P. T.; Dybing, F. Institute of Pharmacology, University of Oslo, Oslo, Norway **Mental and psychomotor effects of diazepam and ethanol.** Acta Pharmacologica et Toxicologica (Kobenhavn). 32(3-4):161-178, 1973.

The performance of eight healthy young males was tested by means of eight psychological and psychomotor tests after the administration of either ethanol, diazepam 10mg or 20mg, or placebo. Diazepam produced stronger subjective sensations of relaxation and reduced concentration than ethanol, whereas the test subjects experienced a similar depressing effect on motivation and effectivity after ethanol and after the largest dose of diazepam. Both diazepam and ethanol reduced the scores in the following tests: memorizing, sorting, complex coordination and critical flicker fusion frequency. Diazepam also reduced the subjects' time evaluation ability, while ethanol did not affect it significantly. Judged by clinical examination diazepam had a less marked effect on proprioception, speech and balance than ethanol. 9 references. (Author abstract modified)

211203 Bruno, Walter. Ospedale Psichiatrico Provinciale "F. Roncati", Bologna, Italy **/Clinical experiments with a new psychotropic drug (Sulpiride)./** Esperienze cliniche con una nuova molecola psicotropa (Sulpiride). Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(6):1321-1329, 1973.

Clinical results obtained in a psychiatric hospital by using sulpiride are examined. The absence of an anxiolotic action in its usage, plus its high tolerance, make sulpiride easily manageable. It is contended that sulpiride eases inhibitions, eliminates delusion and serves as a stimulant. Three cases in which sulpiride was used are described. 6 references. (Author abstract modified)

211361 Inanaga, Kazutoyo; Isozaki, Hiroshi. Department of Neuropsychiatry, Kurume University School of Medicine, Japan **The effects of medazepam (S-804) on all night sleep.** Clinical Psychiatry (Tokyo). 16(1):89-94, 1974.

The effects of medazepam (S-804) on full night sleep were assessed in four healthy adults administered 30mg of this drug 30 min before bedtime. A significant prolongation of total sleep time was noted. The proportion of time spent in each sleep state was unchanged. Subjects experienced no unpleasant feelings after awaking from drug induced sleep. 18 references.

211470 Trimble, M.; Chadwick, D.; Reynolds, E. H.; Marsden, C. D. Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF **L-5-hydroxytryptophan and mood.** Lancet (London). No. 7906:583, 1975.

Mood changes in seven neurological patients after the intravenous administration of L-5-hydroxytryptophan (5-H.T.P.)is reported in a letter. Although none of the patients

had any affective disorder previously, one patient became nauseated, depressed and weepy, while seven other subjects became increasingly distracted or elated. It is concluded that elevation of mood dominates, but results of effects were variable. Other neurological side-effects were seen after doses of 200mg 5-H.T.P. and above, and are discussed in detail; no patient became overtly manic or psychotic. These results are compared to those noted in previous studies. The neurological and psychological effects of the drug are comparable to reactions to other regimens. More properly controlled studies of the effects of intravenous 5-H.T.P. and peripheral decarboxylase inhibition are recommended. 4 references.

211745 Evans, Michael Allan. Indiana University **Clinical studies with marihuana and dextroamphetamine combination. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-1694 HC$13.50 MF$5.00 220 p.

To investigate the possibility of marihuana - amphetamine interaction in man, experimental protocol and psychometric test equipment were established to quantitatively measure drug induced behavioral changes. Higher doses of marihuana - amphetamine combination may produce harmful psychological and cardiovascular effects but not above that of simple addition. The use of stimulants failed to alleviate the performance decrements produced by marihuana smoking, suggesting that THC impairment is not related to sedation or fatigue. (Journal abstract modified)

211831 Kelly, Sean Francis. Boston University Graduate School **The effects of cannabis intoxication on primary suggestibility. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 75-14 HC$13.50 MF$5.00 157 p.

The effects of marihuana intoxication on primary suggestibility were studied in 35 undergraduates. Major findings were that the drug produces a degree of enhancement quite similar to that seen following hypnotic induction and that produced by LSD-25 and by mescaline. The drug produced a significant enhancement of challenge suggestibility. Marihuana's effect on primary suggestibility and imagery suggestibility was clouded by methodological problems. (Journal abstract modified)

212281 Rogliani, G.; Bilotta, M. Ospedale Psichiatrico Provinciale di Napoli "L. Bianchi", Naples, Italy **/Molecular mechanisms of memory and learning (general considerations and clinical applications)./** Meccanismi molecolari della memoria e dell' apprendimento (considerazioni generali ed applicazioni cliniche). Ospedale Psichiatrico (Napoli). 41(2):337-344, 1973.

The molecular mechanisms of memory and learning were investigated in 40 oligophrenic patients treated with commercial preparations based on nucleotides, vitamin B12 and folic acid. Twenty Ss, serving as controls, were treated with a polyvitamin complex. In over 70% of the cases treated, there was a clear improvement in the results of psychometric tests. 12 references.

212495 Hoc, J. no address **/Clinical study and followup of 40 psychotic patients on perphenazine enanthate./** L'etude clinique et follow-up de 40 patients psychotiques sous enanthate de Perphenazine. Ars Medici (Nivelles). 27:2031-2035, 1972.

A clinical study of 40 patients on perphenazine enanthate is reported with a followup. The drug, the ether salt of a heptanoic acid, was characterized by a lasting action after intramuscular injection. A preliminary study used 100mg/day for 15 days. Ten cases of anxious psychoneurosis, 16 of paranoid schizophrenia, 8 cases of manic-depressive psychoses and 10 "character" psychopathies were tested. All patients were male and between 16 and 61. Of the sample tested, 38 patients left the hospital, 27 were rehabilitated and returned to work, and 7 case outcomes were unknown. Among the anxious psychoneurotics, there were nine cures. Doses were 300mg, 100mg and 50mg fortnightly for schizophrenia, anxious neuroses, and cyclothymia, respectively. Prognosis is considered favorable, and higher than that obtained with other drugs. Side-effects were minimal and easily corrected by antiparkinsonian medication.

212774 Audisio, M.; Mazieres, H.; Pisarz, A.; Membrey, J. - M. Centre Psychiatrique de Rouvray, 4, rue Paul-Eluard, 76301 Sotteville-Les-Rouaen, France **/Therapy and long-acting neuroleptics./** Relation therapeutique et neuroleptiques a action prolongee. Evolution Psychiatrique (Toulouse). 39(3):623-641, 1974.

A series of six observations are presented as part of a pharmacological, psychodynamic and ethical discussion of neuroleptics (fluphenazine, in particular). Major factors under observation were the length of the patients' experience, the observational limits, the fact that each patient had used three forms of the drug (incisive, ordinary, and prolonged). Of the six cases observed, three believed in the medication in one sense or another; one reacted negatively; the other two showed no response. The practitioner is cautioned to keep in mind the nonpharmacological effects that a drug may have on the specific patient under treatment.

15 TOXICOLOGY AND SIDE EFFECTS

205603 Thomasova, E.; Mlcakova, K.; Kumpel, Q. Psychiatric Hospital, 746 33 Opava, Czechoslovakia **Confusional states in elderly mental patients treated with antidepressants.** Activitas Nervosa Superior (Praha). 16(3):189-190, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, analyzes the effects of individual drugs on the incidence and extent of the confusional delirious syndrome in patients treated with antidepressants in the gerontopsychiatric ward. Confusional states as a complication of treatment occurred in 11%. All these patients had been treated with amitriptyline in routinely given doses: four in combination with nortriptyline, four with neuroleptics and one patient in combination with a tranquillizer. In patients with a confusional state, increased agitation and delirious experiences' were observed. In four cases the confusional delirious state was complicated by somatic illness, most frequently bronchopneumonia (one patient died). 6 references.

205611 Vinarova, E.; Zamrazil, V.; Nemec, J.; Vinar, O.; Bednar, J. Institute of Psychiatry, Prague 8, Czechoslovakia **Lithium treatment and thyroid function in man.** Activitas Nervosa Superior (Praha). 16(3):198-199, 1974.

At the 16th Annual Psychopharmacological Meeting, an investigation of the possibility of the treatment of thyreotoxicosis with lithium was reported. An attempt was made to find out whether and what changes do occur in the thyroid functions. At the first examination, one patient was clinicaliy hypothyroid, 13 patients had obvious goiter and only in two patients was the thyroid gland not palpable. At the second examination statistical significant differences in enlargement of neck circumference and prolongation of Achilles tendon reflex were found. Two further patients were clinically hypothyroid and in another three patients nodulisation of thyroid gland was found. 8 references.

205612 Marhold, J.; Zimanova, J.; Lachman, M.; Kral, J.; Vojtechovsky, M. Hospital for Mental Diseases, 411 85, Horni Berkovice, Czechoslovakia **To the incompatibility of haloperidol with lithium salts.** Activitas Nervosa Superior (Praha). 16(3):199-200, 1974.

At the 16th Annual Psychopharmacology Meeting, three case studies which support the hypothesis charing an incompatibility between haloperidol and lithium sales were presented. The neurotoxicity of this combination has affinity to the extrapyramidal system and to other regions of the central nervous system. The severeness of complications appears to be proportional to the basal daily dose of haloperidol. 4 references.

205620 Vanecek, J.; Fink, Z.; Vinar, O. Department of Pharmacology, Charles University, Prague, Czechoslovakia **The problem of side effects of thymoleptics.** Activitas Nervosa Superior Praha). 16(3):208-209, 1974.

A paper presented at the 16th Annual Psychopharmacological Meeting, describes an investigation of the problem of side-effects of thymoleptics. The frequency of adverse reaction to individual compounds was too low to permit conclusions. Iprindol is to such an extent hepatotoxic and has such a negative effect on hemopoiesis that it has been put on the list of particularly dangerous substances. In a similar way the teratogenic effects of imipramine is being studied on a worldwide scale, though this suspicion may apply also to other substances of this group. The cardiotoxicity of thymoleptics represents a serious factor. This limits the use of these compounds in patients with cardiovascular disturbances; at the same time higher age groups reveal a high percentage of depression.

205882 Dandoy, Jean-Pierre. no address **/Neuroleptic drugs and automobile driving./** Neuroleptiques et conduite automobile. Lille, 1973. 110 p.

The effect of neuroleptic drugs on driving an automobile was investigated. The necessity of furnishing appropriate medical information as to the side-effects of prescription drugs concerning automobile driving is emphasized. The type of neuroleptic drugs most often used are reviewed, the faculties necessary for driving an automobile are analyzed, and experiments on the driving abilities of Ss who have ingested such drugs are described.

207155 Geering, J. M.; Ruch, W.; Dettli, L. Universitatskinderklinik, Romergasse 8, CH-4005 Basel, Switzerland **/Diphenylhydantoin intoxication due to diphenylhydantoin-isoniazid interaction./** Diphenylhydantoin-Intoxikation durch Diphenylhydantoin-Isoniazid-Interaktion. Schweizerische Medizinische Wochenschrift (Basel). 104(35):1224-1228, 1974.

A case of severe iatrogenic diphenylhydantoin intoxication, attributed to diphenylhydantoin - isoniazid interaction, is reported. On the basis of analysis of the plasma concentrations of the drug in the patient and additional pharmacokinetic experiments, it was demonstrated that the intoxication was due to competitive inhibition of diphenylhydantoin metabolism due to the simultaneous administration of isoniazid. The clinical significance and mechanisms of this interaction are discussed. 16 references. (Author abstract modified)

207196 Modestin, J. Psychiatrische Universitatspoliklinik, Hugelweg 2, 3000 Bern, Switzerland **/On the pathogenesis of delirious states./** Zur pathogenese deliranter Zustande. Confina Psychiatrica -- Borderlands of Psychiatry (Basel). 17(1):42-52, 1974.

The pathogenesis of delirious states was investigated. Occasionally delirious, toxic - confusional states have been observed during administration of various psychotropic drugs. It is suggested that such deliriums are essentially atropine like psychoses induced by an anticholinergic component of the drugs. On the other hand, an enhancement of the central sympathetic tonus as an expression of central vegetative imbalance is considered as a possible explanation for the development of delirious states due to the withdrawal of alcohol and/or drugs. Both hypothesis were tested, and the first hypothesis was confirmed; the second was not. 39 references. (Author abstract modified)

207519 Nishikiori, Takeshi. Toyogo Hospital, Department of Neuropsychiatry, Japan **Side-effects of imipramine and amitriptyline.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(4):395-403, 1974.

The occurrence of an unusal erythematous dermatitis in patients under treatment with imipramine and amitriptyline is discussed. In a sample of 74 patients with endogenous depression and under treatment with these drugs, 5% evidenced a form of dermatitis manifested as a rash of red to red brown color consisting of numerous small lesions appearing in various densities over much of the body. All patients with this disorder were females with a previous history of allergic disease. The eruption occurred a week or more after the initation of imipramine of amitriptyline treatment. Antihistamines were effective in reducing the rash in only one patient. Discontinuation of treatment successfully eliminated the disorder in the rest of the patient sample. 57 references.

207533 Sicard, J. P.; Reignier, A.; Bakouche, P. no address **/Extrapyramidal manifestations due to Metoclopramide in six case studies./** Manifestations extrapyramidales dues au Metoclopramide. A propos de 6 observations. Nouvelle Presse Medicale. 2:31-32, 1973.

Five women and a 14-year-old girl were treated for dyspepsia with daily doses of 20-60mg of Metoclopramide. The crises appeared 24-48 hours after the institution of treatment. Various extrapyramidal side-effects are described. Intoxication of nursing children with Metoclopramide is reasonably frequent as in some countries the product is prescribed as an antiemetic.

207718 Watanabe, Shosuke; Taguchi, Kanzo; Nakashima, Yoshihiko; Ebara, Takashi; Iguchi, Kinya; Otsuki, Saburo. Kawasaki Medical College, Kurashiki, Japan **Leukocytosis during lithium treatment and its correlation to serum lithium level.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 28(3):161-165, 1974.

The correlation between leukocytosis induced by lithium and lithium level in serum is discussed. Leukocytosis was studied in 33 patients receiving lithium salts for the treatment of affective psychosis. Leukocytosis was found to have occurred in 13 cases of which six were of transient form, five cases were of persistent form and two cases of unknown type. The nature of the leukocytosis was a combination of slight leukocytosis with distinct neutrophilia and lymphopenia. No apparent lithium correlation was found between the occurrence of leukocytosis and serum lithium concentration. Changes in the steroid metabolism seem to be responsible for the onset of the mechanism and the reactivity of individuals seems to be a more important causative factor. 12 references. (Author abstract modified)

207768 Van Putten, Theodore. UCLA School of Medicine, Los Angeles, CA **The many faces of akathisia.** 16(1):43-47, 1975.

The clinical importance of akathisia, a common side effect of neuroleptic therapy, is discussed, and means by which the clinician can detect it are considered. Characteristics, frequency, variations, and consequences of akathisia are reviewed. It requires immediate treatment with antiparkinsonism agents and, when possible, a reduction of neuroleptic dosage. Failure to treat the patient may lead to a refusal to continue with prescribed neuroleptic drugs, sudden departures from the hospital, parodoxical responses of phenothiazines, and, at times, exacerbations of psychosis. 16 references.

208536 McCawley, Austin; Shachnow, Norman K.; Mandell, Stanley. St. Francis Hospital, Hartford, CT **Survival in lithium intoxication, status epilepticus, and prolonged coma.** New York State Journal of Medicine. 75(3):407-409, 1975.

The case of a patient with lithium intoxication is described which is noteworthy because he survived following a prolonged coma and multiple grand mal seizures and sustained no demonstrable neurologic deficit. Several aspects of the patient's history are noted, including the high doses of lithium, the high serum levels, and the time lag between discontinuation of medication and onset of neurologic symptoms. 10 references.

208970 Dotti, Andrea; Loriedo, Camillo. Universita di Roma, Istituto di Psichiatria, Rome, Italy /**A contribution to the study of chronic amphetamine psychosis.**/ Contributo allo studio delle psicosi amfetaminiche croniche. Rivista di Psichiatria (Roma). 9(1):63-77, 1974.

Based on three case studies, it is concluded that the use of amphetamines is more likely to result in chronic amphetamine psychosis (a personality disorder) than in schizophrenic psychosis. The megalomanic state of the amphetamine user is emphasized. 16 references. (Author abstract modified)

209018 Schulze, Bernhard. IV. Psychiatrischen Abteilung, Allgemeines Krankenhaus Ochsenzoll, D-2000 Hamburg 62, Langenhorner Chaussee 560, Germany /**The clinical relevance of photosensitivity in psychiatric EEG diagnosis.**/ Zur klinischen Relevanz der Fotosensibilitat in der psychiatrischen EEG-Diagnostik. Nervenarzt (Berlin). 45(4):207-210, 1974.

The clinical relevance of photosensitivity (PhS) in pathologic electrocerebral reactions in psychiatric patients is discussed. The results show PhS present in 4.3% of the cases during systematic exposure to a flickering light. Four out of 40 patients were epileptics and an additional four were photosensitive patients who suffered grand mal attacks due to drugs. Fourteen out of 40 had a myoclonic reaction; two of these reactions also appeared spontaneously. Seven out of 40 patients showed existing functional vasomotor, or organic cerebral alterations. Pharmacotoxic influences and PhS were evident in 36 out of 40 patients. These fell into two groups: a) 21 patients showed PhS under psychopharmacological treatment (especially the tricyclic thymoleptics); b) 13 patients with drug and alcohol misuse showed PhS pathologic reactions even long after withdrawal. These findings support the routine application of photostimulation as indispensible for differential diagnosis and control of psychiatric illnesses. 27 references. (Author abstract modified)

209063 Rizzola, N.; Rosadini, I. Istituto di Psichiatria, Universita di Genova, Genoa, Italy /**Psychopathogenic aspects in acute psychoorganic syndromes (Relationships between drug dependence and delirium tremens type syndromes).**/ Aspetti psicopatogenetici nelle sindromi psicorganiche acute (Rapporti tra farmacodipendenza e sindromi tipo delirium tremens). Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(3):539-553, 1973.

The relationships between drug dependence and syndromes of the delirium tremens type were discussed, and were illustrated by the case of a woman presenting with delirium tremens type symptoms. The S did not drink to excess, but tended to use certain drugs, such as benzodiazepines, quite often. After a trip to her home in Germany where she ceased taking hypnotics and tranquilizers but began taking an excessive number of analgesics, the delirium tremens type symptoms began. The difficulties of heterosexual and social adjustment with this S seemed to be resolved in the reinforcement of earlier oral and anal tendencies with sadomachistic tendencies. 17 references.

209073 Garattini, S.; Morselli, P. no address /**Interactions between drugs.**/ Interazioni tra farmaci. Milan, Ferro Edizioni, 1973. 181 p. Lire 4500.

The possible interactions between drugs when they are administered in combination are examined. The simultaneous administration of two drugs can result in neutralization; can affect the intestinal absorption of one of the drugs; can alter the hematic level; can interfere in the metabolism of the drugs acting on the specific microsomal enzymatic systems; and can interfere on the level of the renal excretion. The following facts are significant as paradigms of the interaction on intestinal absorption and plasma connections: the reduction in absorption of chlorpromazine and tricyclic antidepressants by antacids with aluminum and magnesium hydroxide bases and by vegetable carbon; the retarded absorption of phenylbutazone by imipramine and desipramine and the inverse phenomenon by haloperidol and meprobamate on ethanol; and the increase, sometimes to toxic levels, of plasma values of hydantoin in response to the action of phenylbutazone and salicylic acid in therapeutic doses.

209234 Vohra, J.; Burrows, G. D. Cardiac Dept., University of Melbourne, Royal Melbourne Hospital, VIctoria 3050, Australia **Cardiovascular complications of tricyclic antidepressant overdosage.** Drugs (Basel). 8(6):432-437, 1974.

Cardiovasuclar complications of tricyclic antidepressant overdosage discussed, and treatment is outlined. Consideration is given to action of tricyclics on the cardiovascular system; attempts to reduce absorption of the drug; management of cardiovasuclar complications in intensive care units; and treatment of respiratory complications and hypotension. 13 references.

209324 Koshino, Yoshifumi; Matsumoto, Kanji; Otsuka, Ryosaku; Ito, Kazuyoshi. no address **A case of nonspecific psychoses which manifested convulsive seizures during lithium therapy.** Japanese Journal of Clinical Psychiatry (Tokyo). 3(6):621-628, 1974.

Convulsive seizures as a side-effect of lithium treatment for atypi psychosis in a 19-year-old girl are analyzed. The girl was treated for predominantly manic symptoms with lithium carbonate, levomepromazine, chlorpromazine, and haloperidol for 1 month. After this period, tremor and myoclonic convulsive seizure were manifested. Lithium treatment was shown to induce more spike wave complex in the electroencephalogram. 32 references.

209410 Yagi, Gohei; Ito, Hitoshi. no address **A case of irreversible extrapyramidal hyperkinesia induced by neuroleptic drugs.** Clinical Psychiatry (Tokyo). 15(7):727-734, 1973.

Irreversible extrapyramidal hyperkinesia induced by neuroleptics in a 45-year-old female schizophrenic is discussed. The patient exhibited akathisia under treatment with haloperidol and trihexyphenidyl. These drugs were replaced by chlorpromazine, which induced a minor akathisia and a restless legs syndrome. Replacement of this drug by propericiazine followed by thioridazine caused serious orthostatic hypotonia accompanied by various somatic symptoms. All drugs were replaced by placebo and neuromuscular symptoms were treated with levomepromazine or clothiapine. Termination of these drugs repeatedly aggravated the neuromuscular symptoms. It is proposed that the neuroleptics adversely affected an existing arteriosclerosis and selectively damaged the extrapyramidal system. 13 references.

209438 DiMascio, Alberto; Klerman, Gerald L.; Prusoff, Brigitte. Boston State Hospital, 591 Morton St., Boston, MA 02124 **Relative safety of amitriptyline in maintenance treatment of depression.** Journal of Nervous and Mental Disease 160(1):34-41, 1975.

Somatic complaints voiced by 212 depressed women under long-term amitryptyline therapy are discussed. These somatic complaints included most symptoms generally attributed as being adverse effects of amitriptyline and other tricyclics. Except for reports of dryness of mouth, all somatic complaints were reduced in frequency and intensity during the course of clinical improvement. When patients relapsed regardless of whether they were or were not on maintenance medication, these somatic complaints returned. Except for dryness of mouth, no relationship between somatic complaints and dosage of amitriptyline was found. It was concluded that amitriptyline is relatively safe. 8 references. (Author abstract)

209998 Dry, J.; Aron-Rosa, D.; Pradalier, A. Service de medicine interne, Hopital Rothschild, 43, Blvd. de Picpus, 75571 Paris Cedex 12 **/The appearance of exophthalmia in the course of lithium carbonate treatment: biological hyperthyroidism./** A propos de l'apparition d'une exophtalmie au cours d'un traitement par le carbonate de lithium: hyperthyroidie biologique. Therapie (Paris). 29(5):701-708, 1974.

The possible relationship between thyroid function and lithium carbonate treatment is discussed. A case report is presented of a patient treated for 15 months with lithium carbonate who developed unilateral exophthalmia due to a pseudotumor of the orbit. One year later, hyperthyroidism was demonstrated, with an increased T4 index, a nonhomogeneous scintiscan, a negative Werner test, and absent LATS. 13 references. (Journal abstract modified)

210077 Maccacaro, Giulio A. no address **/Thalidomide and the power of the pharmaceutical industry./** Il talidomide e il potere dell'industria farmaceutica. Milan, Ed. Feltrinelli, 1973. 250 p. 2500 Lire.

The effects of thalidomide taken by pregnant women on their unborn fetuses are described. It is noted that the pharmaceutical companies involved compensated the victims in various countries, but not in Italy. A strong criticism of the medicine and those who administer it, including pharmaceutical companies, is offered.

210136 Ranty, Y. no address **/Three cases of anejaculation in patients treated with clomipramine./** A propos de 3 cas d'anejaculation chez des malades traites a la Clomipramine. Clermont Medicale (Clermont-Ferrand). Annual supplement:159-165, 1973.

Three cases of anejaculation with presistance of desire and erection were reported in depressed patients treated with clomipramine (Anafranil). Impotence is attributed to hyperstimulation of adrenergic structures, and clomipramine's effect on the tryptaminergic and noradrenergic systems, is said to create an emotional decompensation and to reactivate aggressiveness. Anejaculation is thus attributed to a fear of being aggressive. The anxiogenic role of anejaculation is discussed in terms of "toxic" consequences and the guilt involved.

210141 Savinel, E.; Stalinickiewicz, G.; Lelievre-Lalligier, A.; Wemeau, J.; Demarcq, J.-M.; Maille, R. no address **/Acute voluntary poisoning by doxepine./** A propos d'une intoxication aigue volontaire par la doxepine. Mouvement Therapeutique (Lille). 18(3):177-131, 1973.

A case of acute intoxication by ingestion of doxepine is reported. The condition was not treated for 36 hours after ingestion; symptoms included coma, convulsions, shock, anticholinergic signs (mydriasis, urine retention, tachycardia), respiratory disturbances, acidosis, and hyperglycemia. Treatment included insertion of tubes for breathing and aided ventilation, treatment of shock, gastric lavage, third degree auriculoventricular dissociation, morlar soda lactate and peritoneal dialysis. The acute anuric renal insufficiency persisted, with severe hyperhydration and hydric restriction. Improvement by the seventh day permitted feeding by probe, and improvement of disturbances in consciousness was evident by the second day after dialysis. Polyneuritis of inferior members and diffuse attacks on the electromyogram were noted and attributed to the direct toxicity of doxepine on the nerves, the role of the uremigenic factor, vitamine B deficiency and prolonged hypotension. 6 references.

210425 Fiorini, G. Ospedale Psichiatrico Provinciale S. Maria della Pieta, Rome, Italy **/Lithium./** Il litio. Lavoro Neuropsichiatrico (Roma). 50(2):171-180, 1972.

The indications, contraindications, side-effects, complications, and poisoning with lithium therapy are reviewed. Lithium therapy is contraindicated with glomerulonephritis, pyelonephritis, or any disease which affects renal function. Some cases of deformed fetuses have been reported when lithium was taken during pregnancy. Lithium levels should be regularly tested in the blood. The most frequent cause of lithium therapy failure is due to the patient's taking the drug irregularly. Side-effects include: gastrointestinal symptoms, tremors, thirst and polyuria, and weight gain. 24 references.

210810 Herha, J.; Obe, G. Psychiatrische Klinik, Freien Universitat, Berlin **Chromosomal damage in chronical users of cannabis: in vivo investigation with two-day leukocyte cultures.** Pharmakopsychiatrie Neuro Psychopharmakologie (Stuttgart). 7(6):328-337, 1974.

Chromosome analyses were performed with 48 h leukocyte cultures of 20 chronical Cannabis users and 20 controls. The frequencies of exchange type aberrations (chromatid interchanges, dicentric chromosomes)can be arranged as followes: controls less than cannabis users less than cannabis users with hepatitis history. The results are discussed with respect to a possible genetic risk of chronical cannabis usage. 19 references. (Author abstract)

210824 Matthews, Charles G.; Harley, J. Preston. Department of Neurology, Neuropsychology Laboratory, University of Wisconsin Center for Health Sciences, Madison, WS 53704 **Cognitive and motor-sensory performances in toxic and nontoxic epileptic subjects.** Neurology. 25(2):184-188, 1975.

Psychometric, cognitive and adaptive ability, motor proficiency, and sensory discrimination measures were administered to adult seizure patients within 36 hours of blood serum determination of diphenylhydantoin, phenobarbital, and primidone. Thirty five subjects in whom at least one of the three drug levels fell within stated toxicity ranges were compared with 28 subjects of comparable age and IQ who were identified by the same procedure to be nontoxic. The toxic group consistently obtained poorer mean test scores, and significant intergroup differences were found on several measures of attention and concentration and on tests of motor coordination and static tremor. 30 references. (Author abstract)

211012 Prouix, Pierre. Clinique Roy-Rousseau, Quebec **/Experiences of a general practitioner among psychiatric patients./** Experience d'un omnipracticien aupres des psychotiques. Vie Medicale au Canada Francais (Quebec). 3(10):1004-1005, 1974.

The main side-effects to medication in psychotic patients are reviewed. The need for physical examination of psychotics is emphasized. Specific effects covered are upper respiratory ailments, dermatological lesions, physiological functions, cardiovascular effects, and extrapyramidal syndrome effects of overdosage. In conclusion, the necessity for close cooperation between general practitioner and psychiatrist is emphasized. (Journal abstract modified)

211360 Hayashi, Yasuaki; Higashi, Tsuneko; Kadota, Koichi. Department of Neuropsychiatry, Okayama National Hospital, Japan **Three cases of chronic chlordiazepoxide intoxication and their withdrawal symptoms.** Clinical Psychiatry (Tokyo). 16(1):77-82, 1974.

Withdrawal symptoms in three cases of chronic chlordiazepoxide addiction are reviewed. Withdrawal symptoms closely mimicked those of chronic meprobamate addiction, though chlordiazepoxide withdrawal is accompanied by fewer and shorter convulsive seizures and a shorter delusional period. Chlordiazepoxide induces physical dependency when taken in doses of more than 80mg/day for more than 1 month. Addiction is best treated by gradual abstinence. 12 references.

211416 Granacher, Robert P.; Baldessarini, Ross J. Massachusetts General Hospital, Fruit Street, Boston, MA 02114 **Physostigmine: its use in acute anticholinergic syndrome with antidepressant and antiparkinson drugs.** Archives of General Psychiatry. 32(3):375-380, 1975.

The use of physostigmine in the diagnosis and management of acute toxic psychosis due to drugs with anticholinergic properties is reviewed. The syndrome of agitation and toxic confusional psychosis associated with peripheral signs of cholinergic blockade is produced by several plant toxins, antispasmodics, ophthalic preparations, and certain proprietary sedatives, as well as antiparkinson medications, antidepressants, and some antipsychotic drugs. Physostigmine, uniquely among the available reversible anticholinesterase agents, can pass the blood-brain barrier to exert central as well as peripheral cholinomimetic actions to reverse this syndrome. Psychiatrists should make more use of this treatment, and be alert to reversible anticholinergic brain syndromes associated with antidepressants and antiparkinson medications, and even with antipsychotic medications. 50 references. (Author abstract)

211425 McDanal, Clarence E., Jr.; Bolman, William M. University of Hawaii, School of Medicine, Leahi Hospital, 3675 Kilauea Ave., Honolulu, HI 96816 **Delayed idiosyncratic psychosis with diphenylhydantoin.** Journal of the American Medical Association. 231(10):1063, 1975.

A case report is presented of a patient with a delayed idiosyncratic psychosis to diphenylhydantoin sodium prescribed for seizures. Other than the development of a schizophrenic syndrome, signs of intoxication were ubiquitous. Two possible reasons for this reaction are stated: it may simply have been an idiopathic drug reaction; or it could be that the patient's mild underlying chronic psychotic process rendered her more sensitive to these side-effects. Due to the popularity of diphenylhydantoin, this would indicate that many patients may be susceptible to a delayed, idiosyncratic reaction. 3 references. (Author abstract modified)

211427 Granacher, Robert P., Jr. Massachusetts General Hospital, Harvard Medical School, Boston, MA **The central anticholinergic syndrome: management with physostigmine.** Journal of the Kentucky Medical Association. 73(3):147-150, 1975.

Over 600 pharmaceuticals and plants with anticholinergic properties which can produce a neuropsychiatric syndrome of psychotic proportions and the clinical features of this central anticholinergic toxicity are examined. This syndrome is rapidly reversed by physostigmine salicylate, but many physicians continue to be unfamiliar with its use. Guidelines for diagnosis and management of the syndrome are presented. 15 references. (Journal abstract modified)

212107 Hartz, Stuart C.; Heinonen, Olli P.; Shapiro, Samuel; Siskind, Victor; Slone, Dennis. 400 Totten Pond Rd., Waltham, MA 02154 **Antenatal exposure to meprobamate and chlordiazepoxide in relation to malformations, mental development, and childhood mortality.** New England Journal of Medicine. 292(14):726-728, 1975.

In a sample of 50,282 offspring of pregnancies lasting at least 5 lunar months malformations were identified before the first birthday, or at death before the fourth birthday, in 6.5%. A total of 1870 children exposed in utero to meprobamate or chlordiazepoxide were compared with those children who were not. No significant differences were found either overall or in specific outcomes; rates were also similar when exposures occurred during the first trimester or at other times during pregnancy. Deaths (from stillbirth to death by the age 4) occurred in 4.4%, and there was no evidence that antenatal exposure to either drug increased the death rate. Finally, as judged by mental and motor scores at the age of 8 months, and intelligence quotient scores at 4 years, there was no evidence that the drugs caused brain damage. 7 references. (Author abstract modified)

212265 Newton, Ray W. Ninewells Hospital, Dundee, Scotland **Physostigmine salicylate in the treatment of tricyclic antidepressant overdosage.** Journal of the American Medical Association. 231(9):941-943, 1975.

The usefulness of physostigmine salicylate in acute tricyclic drug overdosage was assessed. Following intravenous administration of physostigmine salicylate for tricyclic antidepressant poisoning in 21 paitents, convulsions occurred in two patients,

and severe cholinergic manifestations occurred in two others. Because of these untoward effects and the very short duration of its beneficial action, it is very doubtful that physostigmine has any place in the routine management of tricyclic antidepressant poisoning. 17 references. (Author abstract modified)

212493 Fourestier, J.; Gacon, J.; Efvan, J.; Le Ster, A.; Morcelet, J.-L. no address **/Salivary scintography: interest in treatment of dry mouth provoked by psychotropic medication.** Scintigraphie salivaire. Interet dans le traitement des bouches seches provoquees par les medications psychotropes. Nouvelle Presse Medicale (Paris). 2:839-842, 1973.

The dry mouth syndrome caused by psychotropic medication is described in detail. The dryness may include the pharynx and may cause farther problems in this area. Sulfarlem's salivary activity was discovered by chance by Lelord. The responses of the parotid gland and those of the salivary glands to psychoactive agents are discussed. Positive results were observed from sulfarlem in 80-90% of the cases.

16 METHODS DEVELOPMENT

206971 Helmchen, H.; Muller-Oerlinghausen, B. Psychiatrische Klinik der Freien Universitat Berlin, 1 Berlin 19, Nussbaumallee 36, Germany **/Longitudinal profiles of the effects of psychotropic drugs from clinico-methodological viewpoints./** Langsschnittprofile der Wirkungen von Psychopharmaka aus klinisch-methodologischer Sicht. Arzneimittel-Forschung (Aulendorf). 24(7):976-980, 1974.

Conceptual and methodological aspects of long-term clinical investigations of psychotropic drugs are described. The following precautions are considered necessary: 1) to differentiate the chronic effects of acute medication from the actions of chronic medication; 2) to investigate the influence of the different strategies of psychotropic treatment on the quality of the remission; and 3) to distinguish clearly between clinical and paraclinical changes under long-term treatment. The relationship between reliability and validity of the collected data is discussed, with emphasis on difficulties due to personal fluctuations. Serious ethical problems might interfere with the development of optimal scientific designs for long-term trials. 39 references. (Author abstract modified)

206980 Debus, Gunter. Psychologisches Institut der Universitat, 4 Dusseldorf, Universitatsstr. 1, Germany **/Arbiter's and self-rating of momentary mood in psychopharmacological longitudinal studies./** Selbst- und Fremdeinstufungen des aktuellen Befindens in psychopharmakologischen Langsschnittuntersuchungen. Arzneimittel-Forschung (Aulendorf). 24(7):996-1001, 1974.

The value of arbiter's ratings and self-ratings of motivational and emotional states in long-term psychopharmacological studies is discussed. Methodological problems are considered, showing results of long-term studies with various psychiatric samples in which adjective checklists for patients and a doctor's rating were used. The results indicate constant reliability (internal consistency) and constant factorial structure of self-report over time. There is a high correlation between self-report and doctor's ratings. Two methods which correlate the ratings and criteria of therapeutic success are described. 16 references. (Author abstract modified)

206984 Netter, P. Institut fur Medizinische Statistik und Dokumentation, Universitat Mainz, 65 Mainz, Langenbeckstrasse 1, Germany **/Survey on and evaluation of the contributions of methodological aspects in the investigation of long-term psychopharmacological drug action./** Zusammenfassung und Wertung der wichtigsten methodischen Aspekte bei der Untersuchung von Langsschnittprofilen der Wirkungen von Psychopharmaka. Arzneimittel-Forschung (Aulendorf). 24(7):1008-1010, 1974.

A symposium on methodological aspects in the investigation of long-term psychopharmacological drug action is summarized. Papers dealt with the following subjects: 1) types and criteria of questionnaires for data collection; 2) strategies of experimental design with respect to sources of bias and criteria for judging therapeutic effects; and 3) factors in statistical evaluation. Experimental contributions of the symposium are grouped according to five correlational approaches represented by Cattell's covariation chart. 2 references. (Author abstract modified)

207042 Neu, Carlos; DiMascio, Alberto; Williams, David. Boston State Hospital, 591 Morton St., Boston, MA 02124 **Saliva lithium levels: clinical applications.** American Journal of Psychiatry. 132(1):66-68, 1975.

It is reported that, despite the literature indicating that saliva lithium levels could adequately replace serum determinations in monitoring patients being treated with lithium salts, this procedure has not received much clinical application. Correlations between serum and mixed saliva and parotid fluid lithium levels were investigated in 20 patients, and the reliability of the procedure was documented. It is suggested that an individual patient's ratio of serum to saliva concentrations be calculated and used as a constant in the determinations. 13 references. (Journal abstract modified)

208983 Cirignotta, F.; Forti, A.; Martinelli, P. Clinica delle Malattie Nervose e Mentali, Universita di Bologna, Bologna, Italy **/Polygraphic evaluation of hypnotic drugs: methodological criteria./** Valutazione poligrafica dei farmaci ipnotici: criterio metodologici. Riv. Sper. di Freniatria e Med. Legale delle Alienazioni Ment. (Reggio). 97(5):1086-1093, 1973.

Various scientific methods used in the evaluation of hypnotic drugs are discussed. Results are reported from polygraphic recordings obtained during nine consecutive nights when a commercially sold hypnotic drug was alternated with placebo. 5 references. (Author abstract modified)

209829 Itil, Turan M. no address **Psychotropic drugs and the human EEG.** Basel, Karger, 1974. 377 p. Vol. 8. L21.80.

The effects of psychotropic drugs commonly used in medical practice today are examined by attempting to quantify their effect on cerebral function, utilizing electroencephalography with sophisticated methods of analysis to study problems of biological availability as well as dose response curves at the central nervous system level. Twenty one chapters prepared by various authorities include qualitative and quantitative information on the effect of a large number of tranquilizers and other drugs upon the EEG during the waking state as well as during sleep. Some of the chapters deal primarily with the study of either evoked potentials on subcortical electrograms after administration of psychotropic drugs in man, while some aspects of the statistical analysis of EEG data are considered separately.

210896 Kanter, Saul L.; Hollister, Leo E.; Moore, Frances. VA Hospital, Palo Alto, CA 94304 **Marihuana metabolites in urine of man: V. characteristics and separation of polar metabolites of delta-9-tetrahydrocannabinol.** Research Commu-

nications in Chemical Pathology and Pharmacology. 10(2):215-219, 1975.

The characterization and separation of polar metabolites of delta9-tetrahydrocannabinol is presented. Extraction of human urine with ether at pH 12 and thin layer chromatography using two solvent systems permitted separation of several polar metabolites of delta9-tetrahydrocannabinol (THC) not previously isolated by these techniques. These metabolites appeared as conjugates and are probably dihydroxy alcohols. 8 references. (Author abstract)

17 MISCELLANEOUS

205633 Stika, L.; Vinar, O.; Kubat, K.; Uxa, M. Pod Marjankou 83, Praha 6, Czechoslovakia **Longitudinal trend in prescribing psychotropic drugs.** Activitas Nervosa Superior Praha). 16(3):230-232, 1974.

At the 16th Annual Psychopharmacological Meeting, a longitudinal trend in prescribing psychotropic drugs was described. It can be seen that the consumption of psychotropic drugs in Czechoslovakia has been increasing in the last years with the exception of stimulants, hypnotics and analgesics. Anxiolytics are of special concern, since they can produce dependence. Their consumption has been growing in Czechoslovakia (with the exception of meprobamate, while their consumption has decreased in Scandinavia. 8 references.

205635 Servit, Z. Institue of Physiology, Czechoslovak Academy of Sciences, Prague 4-Krc, Budejovicka 1083, Czechoslovakia **Psychotropic and antiepileptic drugs.** Activitas Nervosa Superior Praha). 16(3):235, 1974.

At the 16th Annual Psychopharmacological Meeting a critical review was given of the history and present state of the research in the field of pharmacotherapy of psychic abnormalities of epileptic patients and antiepileptic effects of psychotropic drugs. Several psychic deviations, especially anxiety and depressive states (phenomena) probably are the symptoms of the epileptic process itself. These are most frequent in the temporal lobe epilepsy characterized by psychomotor seizures. New antiepileptic drugs, quite different from the classic groups of barbiturates, hydantoins and succinimides are derived from the large family of psychotropic agents. The benzodiazepines and carbamezepine are typical examples. Physiological mechanisms of the activity of hypothetical synaptic transmitters in the central nervous system, physiological pharmacology of behavioral phenomena and some relations between psychotropic effects of drugs and seizure susceptibility are reviewed.

206377 Nash, Harvey; Stone, George C. School of Social and Behavioral Sciences, California State College, Dominguez Hills, CA 90747 **Psychological effects of drugs: a factor analytic approach.** Journal of Nervous and Mental Disease. 159(6):444-448, 1974.

Factor analysis was employed to reanalyze the data of a previously reported experiment on the human psychological effects of amphetamines, barbiturates, and amphetamine - barbiturate combinations. The reanalysis both confirms and further illuminates the previously reported findings. Methodological implications are discussed. 2 references. (Author abstract modified)

206437 Usdin, Earl; Snyder, Solomon H. no address **Frontiers in catecholamine research. Proceedings of the Third International Catecholamine Symposium.** Oxford, Pergamon, 1974. 1219 p. L20.00.

Lectures presented at the Third International Catecholamine Symposium in Strasbourg in 1973 are reported. Topics include: 1) the impact of monoamine research on drug development; 2) the synthesis and breakdown of the catecholamines; 3) regulating mechanisms of the catecholamine synethesizing enzymes; 4) drug receptor interactions; 5) function of the adrenergic nerve terminal; 6) catecholamines in central nervous systems; 7) research on amphetamines and centrally active drugs such as neuroleptics, morphine and others; and 8) studies of the role of catecholamines in various psychiatric disorders.

206605 Modell, Walter. no address **1974 drugs of choice 1975.** St. Louis, Mo., C. V. Mosby, 1974. 832 p.

Forty one different contributors report on current drug usage in order to aid in prescribing the right drug for the right situation. In addition to a general discussion in the specialized chapters, a drug index gives both the trade name and generic name of each drug listed. Dosage form and route of administration are defined. Another index gives quick access to the therapeutic problem and the suggested solution.

206940 Mason, Aaron S. Eastern State Hospital, 627 West Fourth St., Lexington, KY 40508 **The psychotropic drug summary.** Diseases of the Nervous System. 36(1):44-45, 1975.

The usefulness of a psychotropic drug summary form in the treatment of psychiatric patients is demonstrated. The form was devised in a Veterans Administration hospital and lists the name of the drug, the daily dose schedule, the total daily dosage and the number of days the patient is on a particular schedule. Target symptoms, response to medication, and side-effects and their treatment are also noted. In addition to being a useful clinical document, the summary can also be used as an educational tool since it highlights the manner whereby the antipsychotic drugs are used inappropriately. This updated summary could be the most essential and valuable document in the medical records of mental patients. 1 reference.

207052 Villeneuve, Andre; Bordeleau, Jean-Marc. no address **The diphenylbutylpiperidines: first North American symposium, 1972.** Quebec, Presses de l'Universite Laval, 1973. 134 p.

Papers presented in Montreal in 1972 at the first North American symposium on the diphenylbutylpiperidines, a new series of neuroleptics synthesized by Dr. Paul Janssen, are provided. The chemistry and pharmacology of long-acting neuroleptics is reviewed, and results of open and double-blind controlled studies of pimozide and fluspirilene by different Canadian clinical investigators are summarized.

207099 Bein, H. J. Departement Forschung, Division Pharmac, Ciba-Geigy AG, 4000 Basel, Switzerland **/Psychopharmacology -- quo vadis./** Psychopharmakologie -- quo vadis. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie (Zurich). 115(1):17-25, 1974.

Future trends in psychopharmacology are predicted, based on the assumption that psychic disorders have a biochemical basis and are essentially the result of deficiencies in the metabolism of biological substances. It is predicted that the psychotropic drugs of the future will be designed to afford a causal treatment for such metabolic disturbances. At present, the practical and theoretical exploration of these possibilities is principally focused on the adrenergic systems of the brain, but it is felt that in all probability other neurological transmitters will be found to be significantly involved in the pathophysiology of psychic disorders. In terms of clinical entities, it is thought very likely that more effective drugs than those now available will sooner be developed for treating depressive states than for treating schizophrenia, within the next 10 years or so. The importance of biochemical investigations in diseases of addiction is discussed with respect to analyzing the effects of psychotropic drugs. 32 references. (Author abstract modified)

207100 Kielholz, P. Psychiatrische Universitatsklinik, Wilhelm Klein-Strasse 27, 4000 Basel, Switzerland /**Future development of pharmacotherapy and toxicomania.**/ Zukunftige Entwicklung der Pharmakotherapie und der Toxikomanie. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie (Zurich). 115(1):27-36, 1974.

The future development of pharmacotherapy and the epidemiology of toxicomania, including alcoholism, are discussed. A Swiss-German joint research project within the World Health Organization is described, which plans to develop a standardized psychiatric classification, exemplified by means of research on depression. Long-term investigations are outlined, which make it possible to judge the psychotropic drugs with respect to the range of indications, the onset of efficacy and the side-effects. Great hope is placed on future biological research. It is noted that alcoholism and drug abuse are still increasing, and intensive interdisciplinary collaboration is recommended. (Author abstract modified)

207161 Greenblatt, David J.; Shader, Richard I. no address **Benzodiazepines in clinical practice.** New York, Raven, 1974. $14.50.

The clinical use of benzodiazepines is evaluated. The chemistry, neuropharmacology, behavioral pharmacology and experimental psychological effects of the drugs are reviewed.

207204 Laborit, H. no address /**Behavior: biology, physiology, pharmacology.**/ Les comportements: biologie, physiologie, pharmacologie. Paris, Masson, 1973. 376p. 200F.

A synthesis of studies from the major sciences contributing to the study of the nervous system and behavioral patterns is presented. The first section discusses the parallels between biochemical structures and morphological ones (mitochondria, membranes, synapses, synaptosomes, etc.), Neurotransmitters such as acetylcholine, catecholamines, serotonin (5-HT), gamma-aminobutyric acid, gamma-hydroxybutryic acid, and other central action amino acids are included in the second chapter. The third chapter deals with anatomophysiological structures, and behavioral groupings are described in chapter four. Cytotoxicity is discussed as an introduction to the fifth chapter on "behaviorotropic" agents. Tolerances and dependancies induced by these agents are also described. The final section reports the general biological basis for reaction to aggression. There is also an attempt to deal with psychosocial and physical aggression by a parallel approach.

207291 Davis, John M. Illinois State Psychiatric Institute, Department of Psychiatry, University of Chicago, Chicago, IL **Dose equivalence of the anti-psychotic drugs.** Journal of Psychiatric Research (Oxford). 11:65-69, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, an empirically determined dose equivalent to chlorpromazine was proposed between different antipsychotic agents. The ratio of all the antipsychotic drugs compared to chlorpromazine given an arbitrary value of 100 was listed. The dose equivalences listed are the mgs of drug necessary to achieve what clinicians feel to be an optimal antipsychotic effect as determined empirically from double-blind studies. The data present an approach to getting an unbiased estimate of relevant potencies and could be used for figures in comparison with relative potencies in various animal preparations such as dopamine blocking properties. 56 references.

207331 Molinoff, Perry B. University of Colorado, Medical Center, Denver, CO **The regulation of the noradrenergic neuron.** Journal of Psychiatric Research (Oxford). 11:339-345, 1974.

At the Symposium on Catecholamines and their Enzymes in the Neuropathology of Schizophrenia held in Strasbourg, France, in May, 1973, the catecholamine biosynthetic pathway was discussed. As more work is done on adrenergic neurons, it appears that regulation takes place at many of the steps of the pathway and by many mechanisms. It is likely that regulatory processes which have not yet been considered will be implicated in the control of the synthesis of the biogenic amines. If catecholamines turn out to be involved in the genesis of one or more of the psychoses, it may be important to understand these regulatory mechanisms both in terms of unraveling the genesis of the disorders and developing the therapeutic approaches. 58 references.

207683 Kupfer, David J.; Detre, Thomas P. Department of Psychiatry, University of Pittsburgh School of Medicine, 3811 O'Hara Street, Pittsburgh, PA 15261 **Psychopharmacologic management of patients: a method for recording treatment decisions.** American Journal of Psychiatry. 132(2):186-188, 1975.

A drug treatment form, the KDS-8, is described which is suitable for use in all types of treatment settings. An important feature is a checklist of treatable target symptoms, with categories of improvement, no change, or worsening. Changes in drug regimen and the clinician's reasons for them are noted. Among the advantages cited are easy retrievability of drug treatment data and the form's suitability for use in audit procedures and research. 4 references. (Journal abstract)

207765 van Praag, H. M. Department of Biological Psychiatry, Psychiatric University Clinic, State University, Groningen, The Netherlands **Neuroleptics as a guideline to biological research in psychotic disorders.** Comprehensive Psychiatry. 16(1):7-22, 1975.

The interrelationship between neuroleptics and biological research in psychotic disorders is examined. It is noted that although biological research in depressions has been greatly stimulated by antidepressants, neuroleptics have played no role of significance in the biological study of psychoses. Depression research has been productive, while the opposite is true for psychoses. A correlation between the therapeutic effect of antidepressants and their monoamine potentiating capacity is cited, along with the research questions prompted by it. Consideration is given to the influence of neuroleptics on the central catecholamine (CA) metabolism, the theory that neuroleptics block CA receptors, the differential influence of neuroleptics on dopamine (DA) and noradrenaline (NA) receptors, the role of DA and NA in regulation of motor activity, and the research strategy of the relationship among neuroleptics, CA metabolism, and the pathogenesis of psychotic disorders. 56 references.

207767 Namyslowska, Irena. Department of Psychiatry, Warsaw Academy of Medicine, Warsaw, Poland **Thought disorders in schizophrenia before and after pharmacological treatment.** Comprehensive Psychiatry. 16(1):37-42, 1975.

Thought disorders were analyzed and classified in a group of schizophrenic patients before and after pharmacological treatment. Two types of thought disorders were found: disturbances of association and of conceptual ability, which do not show intercorrelation. Disturbances of association in schizophrenia are more pronounced than disorders of concep-

tual thinking. Disorders of conceptual thinking are less pronounced and less homogeneous than disturbances of association; only 50% of the schizophrenic population was characterized by them. At the same time, these disorders are more stable features of the functional deficit in schizophrenia than disturbances of association; they changed to only a small extent due to the pharmacological treatment. 30 references. (Author abstract modified)

207921 Crane, George E. Spring Grove Hospital Center, Catonsville, MD 21228 **Two decades of psychopharmacology and community mental health: old and new problems of the schizophrenic patient.** Transactions of the New York Academy of Sciences. 36(7):644-657, 1974.

The use of neuroleptic drugs and the delivery of mental health services in the community is discussed. The massive use of neuroleptic drugs for all mental patients, especially those with schizophrenia, has resulted in help for some, and less time spent in the hospital and outpatient care, but in permanent neurologic disorders in a high percentage of others. Damage has been the result of inadequate monitoring of adverse reactions in patients. The role of the medical profession and of research and regulatory agencies is discussed. In an attempt to shift the emphasis of mental health care from the large institution to the community center or to the patient's home, drugs have been used in quantity. When drugs are no longer effective or when a critical episode occurs, chaos results, often throwing the patient back into society unprepared and a problem for the social services and for law enforcement agencies. 28 references.

207922 Cole, Jonathan O. McLean Hospital, Belmont, MA 02178 **/Psychopharmacology, community mental health and the schizophrenic patient./** Discussion of Dr. Crane's paper. Transactions of the New York Academy of Sciences. 36(7):658-662, 1974.

A discussion of Dr. Crane's paper on psychopharmacology and community mental health is presented. It is felt that, contrary to Crane's view, schizophrenics do well in the community if supported by both drugs and aftercare. Side-effects like tardive dyskinesia affect only about 5% of the hospitalized patients who are treated with drugs. It is agreed that careful data should be collected and the short-term and long-term effects of drugs should be analyzed before patients are treated. It is felt that community care is preferable to that received in a chronic institution. Particular note is made of the decrease in patients in state institutions. There is still a need for institutional care for the dangerous psychotic but the use of community delivery of care can reduce the need for psychiatric hospital beds by 75%. 5 references.

208761 Takahashi, Jun. Takahashi Mental Hospital, Takahashi, Japan **Psychiatric investigation of drug dependence.** Asahikawa Seishin Eisei (Asahikawa). 17:10-14, 1973.

Types of psychoactive and psychotoxic materials are discussed. Typ of stimulants and organic solvents, their pharmacological effects, and clinical symptoms induced by poisoning or dependence are described. The relationship between social phenomena and prevalence of drug dependence is also considered. 4 references.

208918 Ananth, J.; Ruskin, R. Department of Psychiatry, St. Mary's Hospital, Montreal, Quebec, Canada **Treatment of intractable depression.** International Pharmacopsychiatry (Basel). 9(4):218-229, 1974.

Treatment of refractory depression, particularly by the enhancement of the antidepressant effects of medications by different techniques, is discussed. Despite the utility of present treatment methods, 10%-28% of depressed patients remain refractory (Bratfos and Haug, 1968; Greenblatt et al.,1964; Smith et al.,1969). As suicide is a relatively high-risk in depressed patients, refractory patients may run even higher risk. Techniques to bolster pharmacotherapy remain hypothetical at this time. The conclusive evidence of the effectiveness of these methods can come from the clinical application of these techniques by the physicians in treating their intractable, depressed patients. 88 references. (Author abstract modified)

208919 Shah, B. K., Kline, N. S.; Angst, J. Research Center, Rockland State Hospital, Orangeburg, NY 10962 **Explicit solution to pharmacokinetic first-order rate constants of maprotilin.** International Pharmacopsychiatry (Basel). 9(4):230-234, 1974.

Explicit equations are derived to obtain first-order rate constants of the assumed Maprotilin pharmacokinetic model following a single oral, or an intravenous dose. The need for excessive computer programming and/or analog computer simulation is abrogated. 4 references. (Author abstract modified)

208921 Reimer, F. Psychiatrisches Landeskrankenhaus, Weinsberg, D-7102 Weinsberg, Germany **/Experience with long-acting phenothiazines in a psychiatric hospital./** Erfahrungen mit Langzeitpsychopharmaka in einem psychiatrischen Krankenhaus. International Pharmacopsychiatry (Basel). 9(4):245-247, 1974.

Psychiatrists and coworkers of a psychiatric hospital were intervie about the advantages and disadvantages of prescribing long-acting phenothiazines. Almost all respondents thought ease of application and reliability of the results were the crucial advantages. The most important disadvantage was that one could only differentiate dosages to a limiteed extent. Poor results are reported with adipose patients and when changing to other drugs. Considerable extrapyramidal and depressive side-effects are often mentioned. 6 references. (Author abstract)

208928 Ostaptzeff, G.; Ostaptzeff, M.; Lavoine, J.-R. Hopital Psychiatrique, 95570 Moisselles, France **/Medicine for freedom or the freedom of medicine./** Medicament liberateur ou la liberation du medicament. Perspectives Psychiatriques (Paris). 2(46):115-120, 1974.

The freedom of a doctor to prescribe, the freedom of a patient to take the prescription, and the use of the prescripiton to stabilize a patient enough to take part in society are discussed. For a patient who only wants relief of symptoms, it is not appropriate to get to the root of psychological problems. The liberating effect of a medicine is evident if it permits a patient to live with greater pleasure and less alienation even if the patient is still obsessive, phobic, etc. The liberating effect of a medicine is always contingent; the same drugs used to surpress psychological problems and enable patients to integrate into society may be used to express a rejection of that same society (opium, amphetamines, barbiturates, LSD, etc.). The appreciation of freedom gained through a drug is relative to what preexisted and to the conventions of society.

209010 Philpott, William H. Fuller Memorial Sanitarium, South Attleboro, MA **The road to Shangri-La is paved with vitamin and psychotherapeutic faddism.** Journal of Orthomolecular Psychiatry (Regina). 3(3):210-212, 1974.

An article praising nutritional therapy is questioned. A reduction of nutritional and psychotherapeutic faddism by chemical survey of nutritional deficiencies, nutritional dependent states, metabolic errors, toxins, and specifically arranged exposure to commonly met foods and chemicals is advocated. Information gained from such studies is said to indicate therapeutic trials of food and chemical avoidances of incriminated substances. Testing and therapeutic trials are recommended to reduce the element of faddism surrounding nutritional therapy and psychotherapy. 1 reference.

209011 Hoffer, A. 1201 CN Towers, Saskatoon, Saskatchewan S7K 1J5, Canada **The orthomolecular controversy.** Journal of Orthomolecular Psychiatry (Regina). 3(3):164-166, 1974.

The American Psychiatric Association's Task Force Report on Megavitam and Orthomolecular Therapy in Psychiatry is criticized as being biased and incomplete. It is maintained that some of the most important literature relevant to orthomolecular therapy was omitted from the study. It is felt that the committee should have included orthomolecular physicians as well as opponents of orthomolecular psychiatry.

209076 Kumar, R. no address **Animal modes for evaluating psychotropic drugs.** Psychological Medicine (London). 4(4):353-359, 1974.

The use of animal models to evaluate the effects of psychotropic drugs is discussed, and guidelines for drug evaluation studies are offered. Animal studies which suggest that amphetamine induced stereotyped behavior is mediated by dopamine are interpreted as indicating that schizophrenia may be related to an abnormality in dopamine metabolism. Behavioral and metabolic classification of manic-depressive disorders by linking observations of animals treated to affect transmitter functions are discussed and the difficulty in the generalization of anxiety and behavior modification studies to animals is noted. Data from biochemical and physiological research on drug dependence are said to demonstrate agreement between human and animal studies. Ways to increase the predictive value of animal response to drug interaction are considered. 43 references.

209098 Iversen, L. L. no address **Catecholamines.** British Medical Bulletin (London). 29(2):1-93, 1973.

Current research on catecholamines is reported. Clinical and scientific aspects of research are discussed with particular reference to: catecholamine release from neurons; the uptake mechanisms for catecholamines; catecholamine metabolism; the central and peripheral catecholamine pathways as visualized by fluorescent histochemical techniques; the role of catecholamines in the central nervous system; and the interactions of prostaglandins with the noradrenergic nervous system. Classification and properties of alpha-adrenoreceptors and the clinical use of alpha-adrenoreceptor and beta-adrenoreceptor antagonists, as well as other drugs affecting catecholamine systems are discussed.

209126 Lion, John, R. Institute of Psychiatry and Human Behavior, University of Maryland School of Medicine, Baltimore, MD 21201 **Conceptual issues in the use of drugs for the treatment of aggression in man.** Journal of Nervous and Mental Disease. 160(2):76-82, 1975.

Clinical pharmacological literature on a variety of medications tha have beed advocated as useful in treating aggressive patients is reviewed, with the diversity of drugs attesting to the etiological diversity of aggression in man. Drugs under discussion include anticonvulsants, lithium, antipsychotic agents, minor tranquilizers, central nervous system stimulants and hormonal agents. Most literature to date has dealt with animals and human models of aggression and lacks conceptual clarity. It is felt that drug treatment should not obscure the need for verbal therapies, and social and environmental factors should always be regarded. 47 references. (Author abstract modified)

209132 Allen, Richard P.; Safer, Daniel; Covi, Lino. Dept. of Psychiatry, Baltimore City Hospitals, 4940 Eastern Avenue, Baltimore, MD 21224 **Effects of psychostimulants on aggression.** Journal of Nervous and Mental Disease. 160(2):138-145, 1975.

Literature on the relation between psychostimulant drugs and aggres in animals and humans is reviewed. Findings indicate: 1) in animals, small and moderate doses of the major stimulants generally either reduce or have no effect on aggression, whereas high doses and chronic moderate to high doses increase aggression in most species; 2) in man, aggression is not produced by major licensed psychostimulants except in doses which produce a paranoid psychosis; 3) children and adolescents with hyperactivity and aggressive behavior usually respond to stimulant medication with reduced fighting, defiance and impulsivity, and effect on aggression may be separate from effect on hyperactivity. Available data on the human response to stimulants suggest a need to better evaluate low dose amphetamine effects on aggression in adolescents and adults. 54 references. (Author abstract modified)

209428 Sim, Myre. no address **Guide to psychiatry.** 3rd ed., Edinburgh, Churchill Livingstone, 1974. 1223 p. L6.

An update of the Guide to Psychiatry (1963) is presented which includes new work done in the field since the original publication. Psychodynamics and psychopharmacology are examined extensively, examining their effects in treatment and psychotherapy. Additional coverage is provided on alcoholism, psychosomatic disease, schizophrenia, legal aspects of psychiatry and child psychiatry.

209753 Appleton, William S.; Davis, John M. no address **Practical clinical psychopharmacology.** New York, Medcom Press, 1973. 162 p.

The clinical application of psychopharmacology is reviewed. Many aspects of the field are covered and the major categories of useful pharmacotherapeutic agents are described. A summary of clinical psychiatry is included to provide a background for the use of psychotropic agents.

209839 Lavyne, Michael; Wurtman, Richard J.; Moskowitz, Michael; Zervas, Nicholas. Lab. of Neuroendocrine Regulation, Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **Brain catecholamines and cerebral blood flow.** Life Sciences. 16(4):475-486, 1975.

Evidence relating brain catecholamines to the control of cerebral blood flow under physiological circumstances and in disease states is reviewed. Experimental studies of this relationship are described, which have utilized two paradigms: (1) the direct application of catecholamines to blood vessels, in vivo or in vitro, and (2) modification of the release or metabolism of endogenous catecholamines by drugs, lesions, or faradic stimulation. 48 references.

210065 Molinego, Luigi. no address **/Introduction to psychopharmacology./** Introduzione alla psicofarmacologia. Padua, Piccin, 1972. 173 p. 6000 Lire.

The basic precepts of psychopharmacology are surveyed. The most commonly used methods for investigating behavioral changes caused by drugs are described. The various groups of drugs are classified and differentiated based on their effect on behavior. The position of psychopharmacology with respect to its contributions in studying problems such as memory, motivation, aggression, and the placebo effect is summarized and discussed.

210069 Pedrotti dell'Acqua, Luca M. no address **/Addiction and psychotropic drugs./** Tossicomania e psicotropi. Milan, Ediz. Giuffre, 1972. 219 p. 2500 Lire.

Drug addiction and psychotropic drugs are discussed from a clinical, chemical, and pharmacological point of view. The international and national control systems which presently regulate the use and distribution of drugs are critically analyzed.

210099 Valzelli, L. Mario Negri Institute for Pharmacological Research **Psychopharmacology: an introduction to experimental and clinical principles.** New York, John Wiley, 1973. 271 p. $14.95.

Methodological and theoretical approaches to the study of drugs and behavior, emphasizing the integration of biochemical, pharmacological, and cellular aspects of psychopharmacology are presented. Special emphasis is on information for phsiological psychologists, behavioral pharmacologists, biologists, and psychotherapists.

210193 Sebens, Jantiena B.; Korf, Jakob. Dept. of Biological Psychiatry, Oostersingel 59, Groningen, The Netherlands **Cyclic AMP in cerebrospinal fluid: accumulation following probenecid and biogenic amines.** Experimental Neurology. 46(2):333-344, 1975.

Levels of cyclic adenosine 3'5'-monophosphate (AMP) in rabbit cisternal cerebrospinal fluid (CSF) determined under a number of conditions is reported. Cyclic AMP in CSF was increased by intraperitoneally administered probenecid; tricylic antidepressant drugs, haloperidol, isoprenaline or L-DOPA did not influence the increase. Cyclic AMP administered intravenously did not penetrate into CSF. Intracisternally introduced isoprenaline, noradrenaline, dopamine and histamine increased the CSF levels of cyclic AMP. Results indicate that cyclic AMP in the CSF is of central origin, that biogenic amines enhance its secretion from nervous tissue, and that it is eliminated by a probenecid sensitive transport mechanism. There seems to be a close relationship between cyclic AMP of brain tissue and of CSF. Central beta adrenergic receptors may be measured in the intact animal by measuring the release of the nucleotide into CSF after intravenous isoprenaline. 29 references. (Author abstract modified)

210220 no author. no address **Tranquillizers causing aggression.** British Medical Journal (London). No. 5950:113-114, 1975.

The discovery that benzodiazepine drugs may enhance rather than subdue aggressive behavior both in animals and man is discussed. Evidence suggests that such reactions may be due to extrinsic factors which may modify drug effect. These factors include group interaction and environmental frustrations. 9 references.

210334 Pichot, P.; Olivier-Martin, R. no address **Psychological measurements in psychopharmacology Vol. 7.** Basel, Karger, 1974. 267 p. Vol. 7. L14.30.

Instruments for psychological measurements in psychopharmacology are described. The most frequently used instruments over the past 20 years are discussed, including self-rated and observer rated scales. Apart from two sections dealing with the problem of semantics and cooperative trials, descriptions are given of a particular scale, its rationale and psychometric properties and the various studies in which the scale is used.

210437 Ballinger, Brian R.; Simpson, E.; Stewart, M. J. Royal Dundee Liff Hospital, Liff by Dundee DD2 5NF, Angus, Scotland **Urinary screening for drugs in a hospital for the mentally subnormal.** Acta Psychiatrica Scandinavica (Kobenhavn). 50(6):619-624, 1974.

Urinary screening for drugs in a hospital for the mentally subnormal is described. Urine specimens were collected from 117 Ss in a hospital and tested for various psychotropic drugs and anticonvulsants. In 12 Ss, prescribed drugs were not detected and in three Ss nonprescribed drugs were detected. Various characteristics of the Ss are described and possible reasons for the discrepancies are discussed. 16 references. (Author abstract modified)

210511 Haase, H.-J. no address **/Therapy with psychopharmaceutic and other psychotropic drugs./** Therapie mit Psychopharmaka und anderen psychotropen Medikamenten. Stuttgart, F.-K.-Schattauer-Verlag, 1972. 391 p. 55.40Fr.

The uses of psychopharmacologic therapy are examined. The effectiveness of psychopharmaceutical agents is discussed, with directions for their use in practice. Practical instruction sheets for the patient, relatives, and the doctor are included.

210794 Nakamura, Kiyofumi. The Second Sunpu Hospital, Japan **A case of pheochromocytoma with schizophrenia like symptoms.** Clinical Psychiatry (Tokyo). 16(11):979-983, 1974.

A case of schizophrenic symptomatology in a case of pheochromocytoma is discussed. The patient was a 53-year-old female with no significant anamnesis who first evidenced hypochondriac and depressive state at age 44 years. The initial symptoms gradually worsened to hypoactivity, hallucination, and delusion, and the patient was diagnosed schizophrenic. In the ensuing years, the patient showed frequent onset of headache, insomnia, and cardiovascular and metabolic disorders. At age 53, the patient began having seizures and evidenced further metabolic deterioration that caused a rediagnosis to pheochromocytoma. Treatment with propranolol hydrochloride rapidly improved the patient's state. 34 references.

210874 Wider, Francois. Lausanne, France **Psychoactive drugs: including combinations.** Dta Processing in Medicine. Vol 3 Basel, S. Karger, 1974. 264 p. $44.

A review of psychoactive drugs drugs is presented. The substances are separated according to their clinical and theraperuical indications into five major groups: tranquillizers, antidepressants, psychostimulants: and psychodysleptics (hallucinogens, psychotomimetics). Each drug is specified with the International Nonproprietary Name, the trivial name, the abbreviated formula, the structural formula and the trade name.

210998 National Drug Information Service. Australian Dept. of Health, P.O. Box 100, woden, A.C.T. 2606, Australia **Some effects of cannabis.** Technical Information Bulletin (Woden). No. 28:12-13, 1974.

Human and animal studies on the possible therapeutic effects of marihuana on the body are briefly noted. Investigations by Dr. Peter Beaconsfield of London suggest that the possible antihistaminic and diuretic effects of marihuana warrant further study.

211435 Blackwell, Barry. University of Cincinnati, College of Medicine, Cincinnati, OH 45221 **Minor tranquilizers: use, misuse or overuse?** Psychosomatics. 16(1):28-31, 1975.

The issues dealing with the utility of modern psychotropic drugs in the treatment of emotional illness are examined from five viewpoints. An examination is made of what drugs are being used, which illnesses are being treated, if drug use is appropriate and, finally, whether there is misuse or overuse, and if so what explanation can be entertained for it. It is revealed that minor tranquilizers are the drugs most often prescribed in general medical practice, with an absolute and disproportionate increase in the use of benzodiazepines. These drugs are probably used mainly for minor emotional states where symptoms of anxiety or depression accompany or simulate physical disease and consideration of factors supports the use of benzodiazepines on grounds of safety, flexibility and compatibility. There is some evidence to suggest overuse which may be mainly accounted for by factors that reinforce the prescribing habits of the physician. 16 references. (Author abstract modified)

211689 Paton, W. D. M. Department of Pharmacology, University of Oxford, England **Pharmacology of marijuana.** Annual Review of Pharmacology. 15:191-220, 1975.

Studies relating to the pharmacology of marihuana which have appeared since 1972 are reviewed. The main new developments have been in the biochemistry of cannabis metabolites, in cellular and toxicological effects, and in a widening of human studies. Topics discussed include chemical structure - action relationships, composition of cannabis and cannabis smoke, forensic techniques for detecting cannabinoids, distribution of delta1-tetrahydrocannabinol (delta1-THC) and its metabolites, cannabinoid metabolism, cellular actions (cell biochemistry and pathology) and toxicity, neurophysiology (particularly the limbic system and the septal area of the brain), and tolerance and withdrawal effects. Human studies have been concerned with perceptual, cognitive and psychomotor effects, the effect of plasma testosterone, therapeutic possibilities, acute and chronic adverse reactions, and sociological studies. The likenesses and disparities between delta1-THC and other lipophiles are discussed. 268 references.

212215 Pichot, P.; Lacassin, J.; Alvez de Souza, W. Clinique des Maladies mentales et de l'Encephale, 100, rue de la Sante, 75014 Paris **/Typology of depressions and therapeutic behavior of psychiatrists./** Typologie des depressions et comportements therapeutiques des psychiatres. Annales Medico-Psychologiques (Paris). 2(4):602-609, 1974.

Nineteen psychiatric services in France were reviewed to see how they dealt with depressive states. The intent of the investigation was to develop a practical symptomology, to help create a clinical diagnosis using I.N.S.E.R.M. nomenclature, and to determine what treatment depression usually received. Responses were statistically divided into types of maladies, frequency of treatment of 'first stage' depressive syndromes and 'all stages'. of the same. In first stages, nonpsychotic depressions were more often treated with amitriptyline than psychotics, and less often with electroshock. Schizophrenics were more frequently treated with chlorpromazine than psychotics but less often with clomipramine. For all stages, nonpsychotic depression was treated most often with diazepam, and more often with amitriptyline than psychotic depression. For schizophrenic depression, the most common prescription was sulpiride and chlorpromazine. It is concluded that it is possible to predict the therapeutic behavior of psychiatrists. However, given the variety of shades of disturbance and types of treatment, the differences having statistical significance in the described experiment were limited. 6 references.

212431 Aleksandrovskiy, Yu. A. Otdel psikhofarmakologii, Moskovskogo nauchno issledovatel'skogo instituta psikhiatrii, Ministerstva zdravookhraneniya RSFSR, Moscow **/Psychopharmacological therapy and the problems of delineating borderline forms of neuropsychic disorders./** Psikhofarmakoterapiya i voprosy vydeleniya pogranichnykh form nervno-psikhicheskikh rasstroystv. Zhurnal nevropatologii i psikhiatrii imeni S. S. Korsakova (Moskva). 74(11):1713-1717, 1974.

Borderline forms of neuropsychic diseases were divided into neurotic levels and psychotic levels by the clinical actions of drugs. Tranquilizers were used because they possess a specific tropicity to psychopathological symptoms of a neurotic variety. Neuroleptic drugs were used because of their effectiveness in treating psychotic conditions. The therapeutic action of psychopharmacological agents was found to be based on their corrective influence on the general links of the functional system conditioning emotional - affective reactivity. Psychopharmacotherapy was, therefore, concluded to be best suited to pathogenetic methods of treatment in patients with borderline cases. 4 references. (Journal abstract modified)

212593 Jospe, Michael Leslie. University of Minnesota **The placebo effect: an integrated analysis of theoretical and research perspectives. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 74-26199 HC$13.50 MF$5.00 445 p.

An integrated and comprehensive analysis of theoretical and research perspectives on the placebo effect is presented. Following an historical review, the physical characteristics of the placebo are treated, revealing that neither theoretical nor empirical approaches have shown that the physical properties have no appreciable influence on the effect. The effect is then examined in nonpatient Ss in a laboratory setting, with particular emphasis on the classical conditioning perspective, effects of placebos on psychometric performance, self-report scales and perception, and hallucinogenic drugs and the placebo effect. The placebo effect in psychotherapy is then subjected to analysis, including the necessary and sufficient conditions for both, the safeguards which must be incorporated into any research in psychotherapy to assure its being more than merely placebotypic, and an analysis of research in which the so called placebo controls were used. Perspectives on some methodological problems in placebo research are also included. (Journal abstract modified)

212888 Silverstone, Trevor; Turner, Paul. no address **Drug treatment in psychiatry.** London, Routledge & Kegan Paul, 1974. 223 p. L4.00.

The general principles, clinical experiences, and recent trends and advances in psychopharmacology are viewed. The

first part deals with general principles, including consideration of neurohumoral transmission in the central nervous system and the social and psychological aspects of drug taking and abuse. The second part is clinical, covering recent advances in neurophysiology and biochemistry of mental illness, and the pharmacology of drugs which may be used.

PSYCHOPHARMACOLOGY ABSTRACTS

Questions about Clearinghouse service should be addressed to:

Psychopharmacology Abstracts
National Clearinghouse for Mental Health Information
Alcohol, Drug Abuse, and Mental Health Administration
5600 Fishers Lane
Rockville, Maryland 20852

For information on subscriptions and the purchase of single copies of the *Abstracts* (Vol. 7 onward), please refer to page ii of this issue.

DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
ALCOHOL, DRUG ABUSE, AND
MENTAL HEALTH ADMINISTRATION
5600 FISHERS LANE
ROCKVILLE, MARYLAND 20852

OFFICIAL BUSINESS
Penalty for private use, $300

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF H.E.W.
HEW 389

NOTICE OF MAILING CHANGE

☐ Check here if you wish to discontinue receiving this type of publication.

☐ Check here if your address has changed and you wish to continue receiving this type of publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Alcohol, Drug Abuse, and Mental Health Administration
Printing and Publications Management Section
5600 Fishers Lane (Rm. 6-105)
Rockville, Maryland 20852

DHEW Publication No. (ADM) 76-150
Printed 1976